

# THE American Journal OF Gastroenterology

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Peptic Ulcer in the Elderly

A Tube to Aid in the Diagnosis  
of Upper Gastrointestinal Bleeding

Gastrointestinal Hemorrhage Due to Typhoid Fever

Ulcerogenic Tumor of Pancreas

*Twenty-fourth Annual Convention  
Los Angeles, California  
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I. Kirsner, J.B., et al.: *M. Clin. North America* 41:499 (March) 1957.

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1. Swartzwelder, J. C., et al.: J.A.M.A., 165:2063, 1957.  
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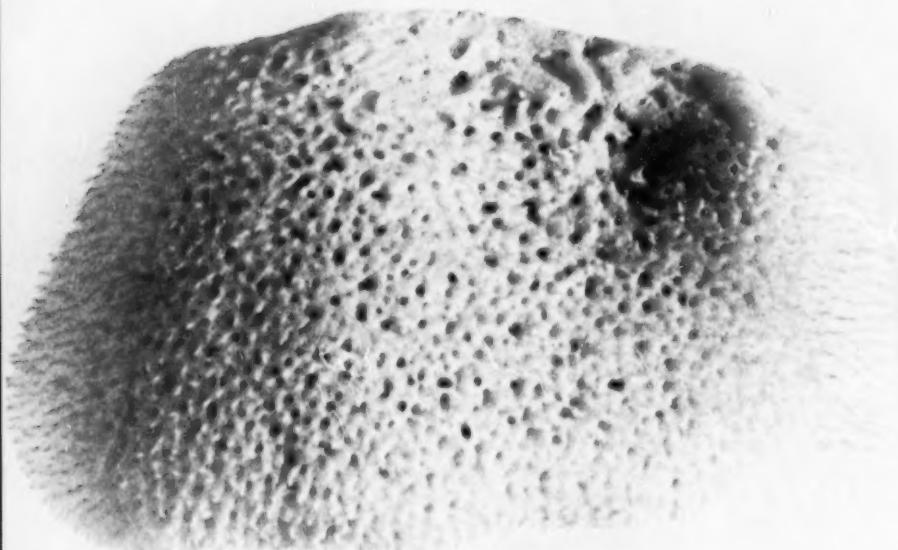
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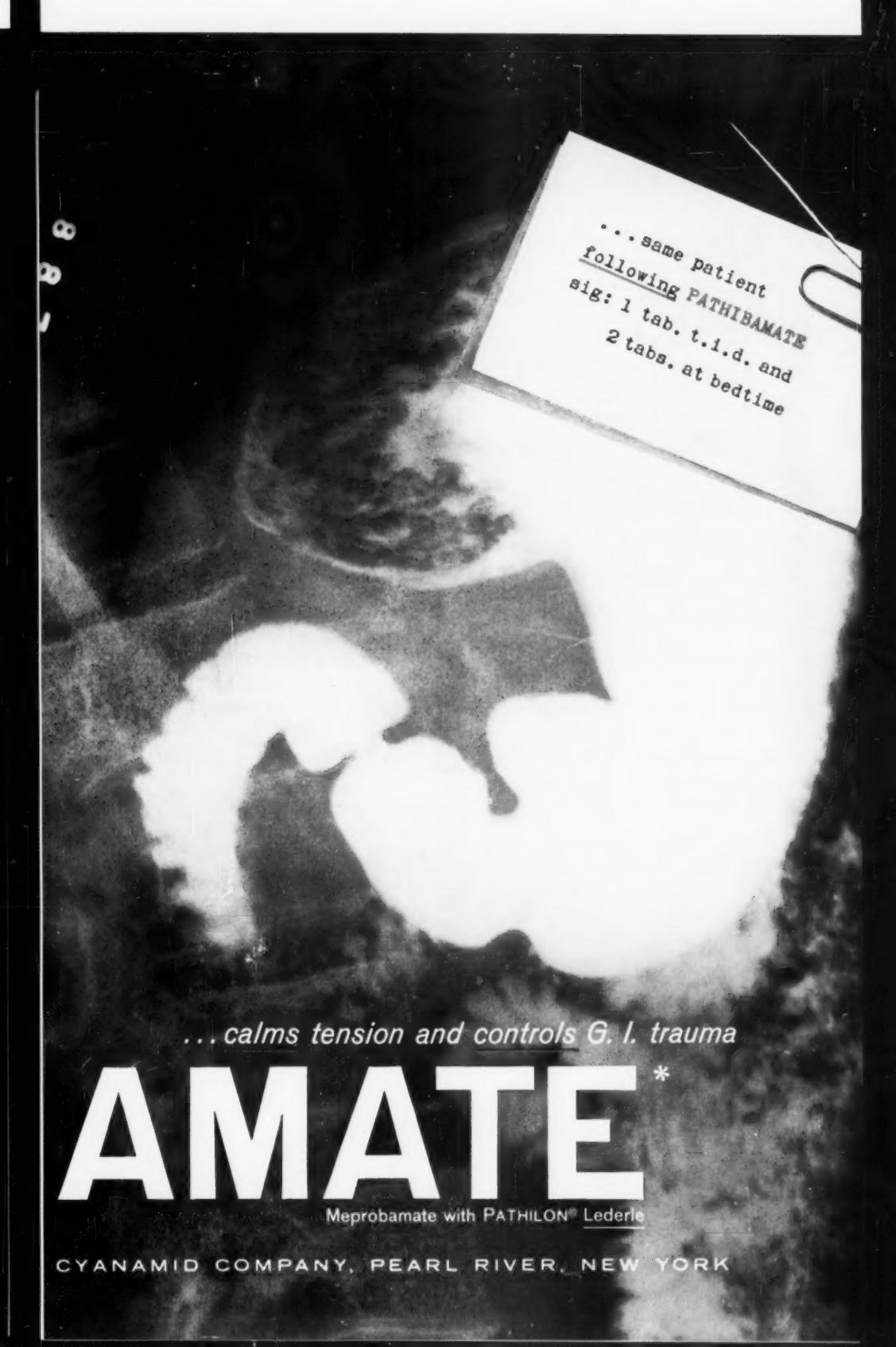
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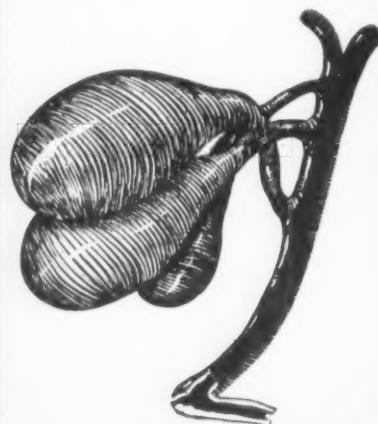
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*Source:* Skilboe, B.: Am. J. Clin. Path. 30:252, 1958.



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(1) Beckman, H.: Drugs: Their Nature, Action and Use, Philadelphia, W. B. Saunders Company, 1958, p. 423.  
(2) Biliary Tract Diseases, M. Times 85:1081, 1957.

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## PEPTIC ULCER IN THE ELDERLY

ABRAHAM I. FRIEDMAN, M.D., F.A.C.G.

Hackensack, N. J.

During the years 1953-56, 62 patients over age 60 were admitted with a diagnosis of peptic ulcer. The diagnosis was confirmed by clinical, roentgen and/or pathologic evidence. The group consisted of 44 patients with duodenal ulcer, 15 with gastric ulcer, 1 with multiple gastric and duodenal ulcer and 2 patients with anastomotic ulcer. The latter were both in males and in one, a recurrence developed following a gastroduodenostomy (Billroth I) and in the other, following a gastrojejunostomy (Billroth II). There were three multiple admissions all with gastric ulcer, 2 because of bleeding. (Multiple admissions are considered as unit admissions.) The average age was 72.0 years ranging from 60 to 91 years. The sex incidence for the group was 46 males and 16 females, 2.9:1, for duodenal ulcer 3.9:1 and for gastric ulcer 1.3:1. The ratio of duodenal to gastric ulcer in the entire group was 2.8:1 (Tables I and II).

The factors of history may be of significance in determining the prognosis of peptic ulceration and have been evaluated. A history of less than 6 months was present in 22 patients, 14 with duodenal and 8 with gastric ulcer. A history of between 6 months and 5 years was given by 12 patients, 9 with duodenal and 3 with gastric ulcer. A history of more than 5 years, in several cases as long as 60 years was present in 26, 20 with duodenal and 6 with gastric ulcer. The periods less than 6 months, more than 6 months and more than 5 years were chosen arbitrarily to subdivide the acute, subacute and chronic peptic ulcer histories.

The most frequent symptoms were those of pain and vomiting. Pain was present in 36 patients (52 per cent) usually epigastric or radiating to the right upper quadrant or to the back. Vomiting was present in 18 patients, 12 with hematemesis. There were no abdominal complaints in 4 patients although 3 presented with hemorrhage and one with perforation. Gastrointestinal hemor-

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From the Department of Medicine, Gastroenterologic Section, Bergen Pines County Hospital, Paramus, N. J.

rhage evidenced by hematemesis or melena or both was a manifestation in 29 patients (48 per cent), 20 with duodenal and 9 with gastric ulcer. In 8 (13 per cent) the hemorrhage was massive, i.e., hematocrit less than 20 per cent, hemoglobin less than 7 gm. and/or RBC less than 2.5 million. One patient with a gastric ulcer and moderately severe portal cirrhosis had multiple admissions, and on 2 occasions, 4 episodes of bleeding. Perforation occurred in 7 patients, 4 with duodenal and 3 with gastric ulcer. Obstruction, however, was present in only 3 patients, all with duodenal ulcer (Table III).

Gastric analysis was performed in 12 patients; 10 with histamine, 2 with modified Diagnex®. Free hydrochloric acid was present in 11 patients; the mean value (for hydrochloric acid) was 47 mEq/l. One patient with a gastric ulcer presented no free hydrochloric acid following the administration of a single dose of .5 mg. histamine base.

TABLE I  
AGE DISTRIBUTION

Decade	Patients
10th	1
9th	10
8th	31
7th	20
Total:—	62

Surgery was performed in 10 patients. Subtotal gastrectomy was done in 5 patients, 3 with gastric and 2 with duodenal ulcer; in the latter, because of hemorrhage and obstruction and in the former, 2 because of hemorrhage and 1 because roentgen diagnosis could not exclude malignancy. Gastroenterostomy and vagotomy were performed in 2 patients, pyloroplasty in 1 and simple closure of a perforation in 2, all patients with duodenal ulcer. The mortality was 1 case (10 per cent). This man, in addition to his uncontrolled hemorrhage from a duodenal ulcer, presented a left hemiplegia, a sequel to a cerebrovascular accident. He died on the 6th postoperative day from paralytic ileus which may have resulted from a mesenteric occlusion. Permission for autopsy was denied.

A total of 13 patients (25 per cent) died while under medical regimen, 7 (13 per cent) because of hemorrhage, 5 from a duodenal and 2 from a gastric ulcer. Four patients died of perforation, 2 with gastric and 2 with duodenal ulcer. In 2 of these patients, a precise diagnosis was not established until necropsy. One, when first seen, was too ill to be operated on, the other, presented no abdominal complaints and no localizing physical findings. One patient died

from a pulmonary embolus and 1 from a myocardial infarction. The latter presented severe coronary atherosclerosis and following moderate blood loss he died suddenly.

#### ASSOCIATED FINDINGS

Moderately severe Laennec's cirrhosis was present in 4 patients, 3 with duodenal and one with gastric ulcer; bleeding occurred in 3 of these patients and was due to the ulcer. Two of these patients bled massively from a duodenal ulcer and died. In 1 of these patients a primary hepatoma was also encountered. One patient presented with hiatus hernia but the source of bleeding was a duodenal ulcer. Cholelithiasis was seen in 2 patients. A past history of pulmonary tuberculosis was present in 5 patients; chest films revealed healed pulmonary lesions. Another patient presented an associated bronchogenic carcinoma. One patient presented with nephrocalcinosis but serum calcium and phosphorus de-

TABLE II  
SITE AND SEX DISTRIBUTION

	Female	Male	Total
Anastomotic		2	2
Gastric ulcer	7	9	16
Duodenal ulcer	9	35	44
Peptic ulcer	16	46	62

terminations were normal. A history of hypertension was elicited in 10 patients. Arteriosclerotic heart disease and hypertensive cardiovascular disease were each present in 4 patients and generalized arteriolar sclerosis in 5 patients. Emphysema and *cor pulmonale* were seen in 1 patient and congestive heart failure in another.

#### DIAGNOSIS AND TREATMENT

Although the matter of diagnosis is not pertinent to the subject of this paper a brief statement of the routine practices leading to a diagnosis are in order. Barium meal examination during the period of active bleeding has been requested more frequently of late. I do not believe, however, that the number of accurate diagnoses have increased appreciably as a result of this ancillary measure. This may be due to a lack of experience. On the other hand two patients bled massively for 24 hours following barium meal examination done with the usual precautions<sup>1</sup>. One of these patients died of a massive hemorrhage from a gastric ulcer. The association may have been purely fortuitous.

The bromsulfalein test during active bleeding has not been a useful, differential, diagnostic procedure in our hands<sup>2</sup>. During episodes of massive bleeding from whatever cause, we have found that bromsulfalein retention is significantly higher than normal and especially so in the aged, with less stable homeostatic factors. Where the diagnosis is equivocal we believe that Blakemore's suggestion<sup>3</sup>, i.e., the introduction of a balloon to exclude esophageal bleeding, is useful. Esophagoscopy was employed during periods of active bleeding on two occasions and served to exclude varices as the cause.

Should the patient be admitted to the medical ward surgical consultation is immediately requested if massive gastrointestinal hemorrhage has occurred. Blood is replaced in adequate amounts in an attempt to maintain the hematocrit between 30 and 35 per cent. In patients with a history of cardiovascular disease packed red blood cells are preferred to whole blood. Patients who suffer from nausea, anorexia or vomiting are maintained in fluid and electrolyte balance by

TABLE III  
COMPLICATIONS

	Duodenal Ulcer	Gastric Ulcer	Total
Hemorrhage	20	9	29
Perforation	4	3	7
Obstruction	3		3
			39

glucose infusions, reinforced with vitamins, etc. Intubation is not practiced unless a diagnosis of obstruction or perforation has been made. A bland low residue diet without meat or concentrated protein is employed in those patients who can tolerate oral feeding. Frequent small feedings are the rule. An antacid combination of aluminum hydroxide gel and magnesium trisilicate is administered in 15 c.c. doses every 2-3 hours during the day and every 4 hours during the night. Sedation has been rarely necessary except for restlessness due to extreme anoxemia; in these patients oxygen is useful although Demerol is not withheld.

#### COMMENT

The onset of peptic ulcer in patients during or after the 7th decade is not adequately appreciated despite several important papers in the literature<sup>4-8</sup>. It is only in the past 15 years that significant reports on peptic ulcer in the aged have appeared. On the one hand, Feldman<sup>7</sup>, reviewing 1,154 cases of duodenal ulcer, found only 16 patients in whom the onset began after age 60. On the

other hand Rafsky, Weingarten and Krieger<sup>6</sup> report that 4.5 per cent or 81 of 1,800 cases with peptic ulcer gave a history that began after the 7th decade. In the present report a history of less than 6 months was given by 22 patients, approximately one-third of the group. An additional 20 per cent gave a history of less than 5 years so that approximately 50 per cent presented a history that began after age 55. It is undoubtedly likely that a modest percentage suffered from duodenal ulcer without prominent symptomatology or prior knowledge of their illness, but one may believe that in the great majority the history is reliable.

The high incidence of duodenal ulcer in the 7th decade is all the more unusual because achlorhydria increases with advancing age. Vanzant et al<sup>9,10</sup> found that in routine studies of patients over age 60 without gastrointestinal symptoms achlorhydria following histamine was present in 27 per cent, 31 per cent males and 21 per cent females. This compares with achlorhydria of less than 1 per cent below the age of 25. Other observers studying large groups of patients found achlorhydria to range from 23-26 per cent over age 60<sup>11,12</sup>. Ivy<sup>13</sup> and his group found that the average mean for free hydrochloric acid diminished from 50 mEq/l before age 50 to 35 mEq/l after age 60. The old dictum "no acid no ulcer", however, still remains an *a priori*. Although in 1 of these patients with gastric ulcer there was no free HCl following a basic dose of histamine the work of Kay and his group<sup>14</sup> indicates that histamine produces a constant and uniform maximum stimulus to gastric secretion only after four times the basic test dose has been administered. In this regard it is important to emphasize that the use of histamine for stimulation of gastric juice requires a definite standard dosage that is infrequently adhered to. The basic dose that should be administered is .1 mg. of histamine base (phosphate) per 10 kg. of weight. The routine performance of the histamine test often fails to employ this dosage and on occasion we have found that therapeutic histamine .01 mg. per ml. was employed for gastric stimulation. The vascular effects of larger doses of histamine may be prevented by the previous administration of an antihistaminic.

Why such a high percentage of patients develop peptic ulcer after age 60 when the average acidity begins to decrease remains a question to be answered. Obviously there is no achlorhydria in these patients although the mean values for hydrochloric acid may be less. Some have postulated decreased resistance of the mucosa due to diminished circulation and arteriolarsclerosis<sup>12</sup>. At the present time studies employing the Wood gastric biopsy instrument may provide a clue by revealing the proportion of parietal cells in gastric mucosa in the aged and their relationship to the quantitative secretion of hydrochloric acid. Since most of the studies on gastric acidity were done in the 1930's the alteration in the character and tempo of our economic and social life may have altered the frequency of achlorhydria and consequently increased the tendency to the development of peptic ulcer in the older age group. A repeat routine survey of gastric secretion in today's general population, 25 years later, would serve to define these factors more clearly.

Complications were present in 65 per cent of this group. In a large series previously quoted 58 per cent presented complications on admission, 40 per cent with bleeding, 10 per cent with pyloric obstruction and 18 per cent with perforation<sup>6</sup>. Hemorrhage in peptic ulcer has been reported occurring in approximately 30 per cent of the hospital ulcer population<sup>4,15</sup>. In this series it was present in 50 per cent. The age of the patients may be important factors in this increase. Unfortunately, we have no adequate clinical record of the incidence of previous bleeding. On the other hand the incidence of perforation is perhaps somewhat lower than is usually reported and perforation occurred almost as frequently with duodenal as with gastric ulcer. Again, obstruction occurred in only 3 patients out of 44 with duodenal ulcer, approximately 7 per cent or lower than the rate ordinarily found in the average group of duodenal ulcer patients. The percentage of complications in this study is at variance with reports that include all age groups.

Another interesting feature in this age group is the greater approach to parity in the incidence of duodenal to gastric ulcer in those patients with a more acute history. Patients with a history of less than 6 months' duration presented a ratio of duodenal to gastric ulcer of 1.7:1 as compared with a ratio of 3.3:1 in patients with a history of 5 years or more. Rafsky, Weingarten and Krieger<sup>6</sup> found that the incidence of gastric ulcer in their series was approximately 2 to 1 and in duodenal ulcer approximately 4 to 1 in favor of the male sex. We have found a ratio of 1.3:1 in gastric and of 3.9:1 in duodenal ulcer in favor of the male sex. The ratio of 4:1 of males to females in duodenal ulcer over age 60 thus is smaller than the ratio of approximately 5:1 in the universal age group.

The high mortality in this group, 25 per cent following a medical regimen, is not unusual, compares with similar reports and is related in part to the age of the patients and to the fact that patients admitted to a county institution may be in a poorer physical condition than those sent to private hospitals. There is often a long history of malnutrition, physical debility, chronic disease and perhaps alcoholism. An accurate history from the patient or relatives occasionally is impossible to obtain. In addition, the well known observation that significant and diagnostic physical signs are often absent in the elderly makes treatment more difficult. Such a high mortality calls for a re-appraisal of current medical practice. In view of the age of the patients and their limited reserves, supportive therapy including adequate blood and electrolyte replacement may not be enough. It is recognized that the medical status of the aged patient, particularly the renal and cardiac system, deteriorates rapidly with active bleeding. In no other group does the mortality rise so greatly with temporizing medical care. The advantages of early surgery are well known and surgical results today are sufficiently excellent to support a more aggressive attitude on the part of medical personnel. Further, the possibility of a recurrence of bleeding and its subsequent hazards provide an additional incentive to surgical intervention. Although we

have been committed recently to such a program one of our problems and in a sense, therefore, iatrogenic, remains that of inducing the surgeon to intervene more actively. The age of the patient appears to be an important influence in the reluctance of the surgeon to adopt a more aggressive attitude.

On the basis of the findings in this and other studies<sup>3-15</sup> it appears advisable to suggest that if hemorrhage does not cease in the first 12 hours that the patient be operated on and that this policy be adopted even though the loss of blood can be replaced adequately.

As a further extension of this "liberal" policy the treatment of patients with a long history of peptic ulcer also requires modification. In view of the low mortality of elective ulcer surgery in capable hands, more liberal indications for subtotal gastrectomy should be exercised in patients over age 50 who bleed from a peptic ulcer. Although the present policy of most gastroenterologists is to delay surgery until after the second hemorrhage there appears sufficient justification to revise this practice in patients over age 50 and to suggest surgery after the first episode of bleeding. Similar liberal indications for surgery in the patient who perforates or obstructs should be advocated. Most gastroenterologists have been reluctant to contemplate such an apparent radical attitude in view of the nonphysiologic character of a subtotal gastrectomy and the frequency of the postgastrectomy syndrome, but the consistently high mortality in these age groups requires a bolder approach. The increase in longevity and the greater incidence of peptic ulcer and its complications we see today require re-appraisal of current medical and surgical practice in the complicated peptic ulcer patient 50 years of age or over.

#### CONCLUSIONS

1. Sixty-two patients with peptic ulcer disease over age 60 were studied. The group consisted of 44 duodenal, 15 gastric, 1 multiple and 2 anastomotic ulcers.
2. More than 50 per cent of the patients in this series apparently presented their first symptoms after age 55. The sex ratio of duodenal to gastric ulcer in those with a more acute history approached unity.
3. Hemorrhage was the most common complication, occurring in almost 50 per cent. Perforation occurred in 7 per cent and obstruction was relatively infrequent.
4. The high mortality, 25 per cent following medical treatment, 13 per cent from hemorrhage, in the patient over age 60 requires an earlier, more aggressive surgical attitude for the complications of peptic ulcer disease. The ulcer patient who presents with hemorrhage or perforation after age 50 should be treated with definitive surgery when conditions permit.

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## A TUBE TO AID IN THE DIAGNOSIS OF UPPER GASTROINTESTINAL BLEEDING

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The surgeon is faced with the problem of evaluating the source of bleeding in a patient who may have multiple lesions. In our experience at this hospital we have found patients with severe liver cirrhosis associated with actively bleeding duodenal ulcers. We have also seen patients with liver cirrhosis and ruptured varices in the fundus of the stomach associated with esophageal varices which were completely inactive.

We are fully aware of the perplexing problem that faces the surgeon when a patient presents himself on admission with massive hematemesis. Sufficient blood is drawn for a complete blood count, hematocrit, typing and cross-matching, blood urea nitrogen and blood sugar. A blood profile to rule out any blood dyscrasias is performed. A bromsulfalein test is also done. An electrocardiogram, as well as an x-ray of the chest are taken. The blood picture is evaluated, and blood loss is replaced in the patient. A complete history and physical examination are performed. The history may, or may not be helpful in ascertaining a positive picture of ulcer disease, or liver cirrhosis, or a composite picture of both. In the physical examination palpation of the liver may, or may not be positive, depending on the stage of the liver disease. With regard to the bromsulfalein test, we frequently encounter high levels for the same reason that we see elevated blood urea nitrogen associated with intestinal absorption of blood.

The classification used in this institution for upper gastrointestinal bleeding cases that require active treatment consists of two groups. The surgical management varies with the different groups.

These groups are:

1. Those lesions above the esophagocardiac junction
  - a. Esophageal varices.
  - b. Ulcerations of the esophagus, peptic ulceration.
  - c. Neoplasms of the esophagus.

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From the Surgical Service of the Coney Island Hospital, John E. Hammatt, M.D., F.A.C.S., Director.

2. Those lesions below the esophagocardiac junction
  - a. Bleeding ulcers of the stomach and duodenum.
  - b. Neoplasms of the stomach and duodenum. (rarely).
  - c. Ruptured varices of the stomach.
  - d. Diffuse gastritis.
  - e. Hemangioma.

In evaluating a patient with massive hematemesis the bromsulfalein test has been found unreliable. Patients with both cirrhosis of the liver and gastroduodenal ulcerations are not infrequent, furthermore, large amounts of blood in the gastrointestinal tract give false bromsulfalein readings. It has also been found that a gastrointestinal series when the patient is actively bleeding may be of little value because:

1. There may be many clots in the gastrointestinal tract which will fill an ulcer crater and make it impossible to visualize a bleeding point.
2. The condition of the patient is such (shock) that it may not be feasible to subject the patient to this procedure.
3. A negative x-ray series is common when the lesion is localized high in the stomach.
4. A positive x-ray for ulcer does not always give the source of bleeding.

It is noteworthy that even the history may be of little value. It may give a false impression. An illustrative case stimulated us to devise the adjunct which is now used routinely in all cases of massive hematemesis. The surgical management depends on the localization of the lesion. A procedure of some kind had to be improvised to differentiate between the source of bleeding from esophagus or stomach.

*Case 1:*—H. B., a 61-year old white male was admitted with massive hematemesis. The condition of the patient was such that a history was unobtainable. He had no living relatives. His landlady was summoned to the hospital and interrogated. The information received from her was that he was a derelict and a drunkard. A bromsulfalein test on admission revealed 37 per cent retention of the dye. A Sengstaken-Blakemore tube was inserted to compress the esophageal walls. In spite of numerous blood transfusions the patient exsanguinated within 18 hours. Autopsy revealed a fresh ulceration of a localized sarcomatous lesion of the posterior wall of the stomach.

From this case it was learned that it is not justifiable to depend on a history or specific laboratory procedures in this type of emergency. Because of the multiplicity of the lesions which may be present in one single case, further investigation is not only advisable, but mandatory. One must immediately look for other means of evaluating this type of critically ill patient.

With regard to the actual surgical procedure *per se*, an exploratory laparotomy in itself may leave the surgeon frustrated because of an inability to locate the specific bleeding point. There are only 2 procedures which may be undertaken in this type of patient.

1. Ligation for esophageal varices.
2. A subtotal gastrectomy for other conditions below the esophagocardiac junction such as bleeding duodenal or gastric ulcer, ruptured varices, in the stomach, diffuse gastritis or hemangioma.

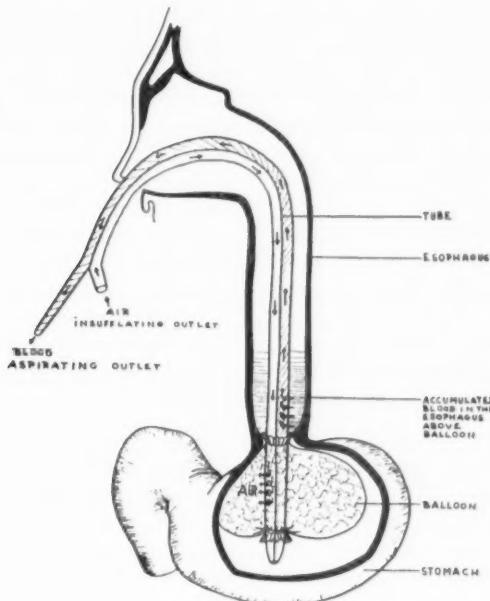


Fig. 1

The decision must be made preoperatively which of these two procedures will be undertaken. A tube is described which we have used successfully in active gastrointestinal bleeding, to differentiate bleeding from the lower end of the esophagus as compared to bleeding below the esophagocardiac junction.

#### DESCRIPTION

There is illustrated a tube (Fig. 1) which we are now using routinely for diagnosis. This is a double lumen tube. One end is blind. The proximal portion of the tube has two openings, one of which is used for aspiration, and the other is used for the insufflation of air into a balloon. At the end of the tube there are

several small openings in the portion which is used for insufflation and open in the balloon. In the other lumen for aspiration, slightly more proximal, there are several small openings. These open into the esophagus. A fine latex rubber is then tied with silk directly below the proximal openings, completely encircling the distal openings, and then tied at the very tip at its blind end and snugly at the proximal one. The tube is then insufflated with approximately 150 c.c. of air to test the efficacy of the balloon.

#### PROCEDURE

The double lumen tube with the collapsed balloon is inserted through the nasal cavity down into the stomach. Through the opening for insufflation 150 c.c. of air is insufflated. The tube is now pulled proximally so that the balloon will rest snugly against the cardia of the stomach. The tube should not fit too snugly lest it may compress esophageal varices if they are present, and it must not fit too loosely lest it may allow for seepage of blood into the stomach around the balloon. At this time 50 c.c. of water is instilled into the opening that is marked "aspiration". For the next 20 minutes this portion of the tube of the esophagus is washed several times and aspirated. There must be a return of the 50 c.c. of water that was previously instilled. If this 50 c.c. of water is not aspirated, then it may be certain that there is a seepage into the stomach, and therefore, the balloon does not fit snugly against the cardia. If this exists, more traction is exerted until return of the injected water is obtained. The aspiration of this lumen is continued constantly during this 20-minute interval and the contents of the aspirated material is noted.

Four cases are reported in addition to the one presented above, each of which presented a different diagnostic problem and in each the diagnosis was pinpointed by our tube as to whether the bleeding was above the esophagocardiac junction or below it.

*Case 2:*—M. S., age 74, white male was admitted with a massive hematemesis and port wine tarry stools. The tube was passed and it was clearly demonstrated that the bleeding was below the esophagocardiac junction. The patient was explored after being transfused. A far advanced liver cirrhosis was found. A fresh bleeding point was found in the first portion of the duodenum from an actively bleeding duodenal ulcer. A subtotal gastrectomy antecolic Hofmeister type was performed. Postoperatively the patient did well and was discharged.

*Case 3:*—C. E., age 64. This well developed colored male was admitted with massive hematemesis and port wine stools. The tube was passed and there was no evidence of bleeding from above the esophagocardiac junction. The patient was explored after multiple blood transfusions. A ruptured gastric varix was found in the specimen after a subtotal gastrectomy antecolic Hofmeister type was performed, and it was also noted that the patient had a marked liver cirrhosis. Patient made an uneventful recovery and was discharged. A blind

gastrectomy was performed because we felt that the bleeding was below the esophagogastric junction. This was confirmed by our operative findings.

*Case 4:*—T. N., age 69. This well developed white male was admitted with massive hematemesis and port wine stools. The tube was passed and it was noted that the bleeding was not present above the esophagocardiac junction. The patient was explored and the only positive findings were a diffuse gastritis and a marked liver cirrhosis. A subtotal gastrectomy was performed. Post-operatively the patient stopped bleeding and was transferred to the medical service for the treatment of his liver cirrhosis.

*Case 5:*—J. S., age 59. This well developed white male was admitted with massive hematemesis. The tube was passed and 150 c.c. of venous type blood was aspirated from above the esophagocardiac junction. The patient was a known case of liver cirrhosis. It was then decided to pass the Sengstaken-Blakemore tube. This was allowed to compress the esophageal wall for 48 hours and was then removed. Bleeding was controlled and patient was transferred to the medical service for treatment of the liver cirrhosis.

Following the test, the tube is taped to the nose. Particularly when emergency surgery is contemplated the tube has the advantages of prevention of aspiration pneumonitis by occluding the distal end of the esophagus. When the tube is used for diagnosis we must be aware of the pressure within the lumen and its effect on the esophageal wall. Too much pressure on the balloon may act as a tamponade and eliminate the purpose of the tube for diagnosis. If the tube is too loose against the cardiac, it prevents separation of the esophagus from the stomach.

It has been difficult to demonstrate in all cases that when bright blood is aspirated that we are dealing with bleeding from esophageal varices. Further attempts to confirm the diagnosis have also been made by injecting 50 c.c. of this opaque substance and taking an x-ray. In all of our cases when no blood was aspirated a diagnosis of gastrointestinal pathology below the esophagus was made.

#### SUMMARY

A double lumen tube is described which has been used successfully in active gastrointestinal bleeding to differentiate bleeding from the lower end of the esophagus as compared to bleeding below the esophagocardiac junction. For this reason a determination of source of bleeding in esophagus or stomach should be done.

## CLINICAL IMPRESSIONS OF A NEW HYDROCHOLERETIC AGENT, ZANCHOL®

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The new hydrocholeretic agent Zanchol® (florantyrone) is a synthetic fluoranthene derivative with a ketobutyric acid side chain. Unlike agents of its therapeutic class derived from natural bile it is nonsteroidal in structure. Descriptively it is  $\gamma$ -oxo- $\gamma$ -(8-fluoranthene) butyric acid.

Animal studies indicate<sup>1</sup> that Zanchol has a high index of safety. The LD<sub>50</sub> per kg. of body weight when given orally is 1,160 mg. in mice and 2,500 mg. in rats. Clinically, we have administered Zanchol to 182 patients over a period of approximately three years in dosages ranging from 500 to 5,000 mg. daily, without evidence of toxicity as determined by repeated physical examinations, blood tests, liver profile studies and urine specimen examinations.

### METHOD AND MATERIAL

This report summarizes our clinical experiences with Zanchol in 182 patients with various biliary disorders. Twenty of these patients were intubated with T-tubes following recent cholecystectomy and common duct exploration; 55 had a diagnosis of postcholecystectomy syndrome; 75 had chronic calculous cholecystitis for which surgery either was contraindicated or refused by the patient; 15, chronic noncalculous cholecystitis (initially 20 patients were diagnosed as having this disorder, but of these, 5 later were shown to have unrelated disorders); 3, serum hepatitis; 2, viral hepatitis; 8, uncomplicated cirrhosis of the liver; and 4, a confirmed diagnosis of cholangiolitis with hepatitis. Many of these patients were seen in private practice, while the remainder were studied on the medical and surgical wards and in the gastrointestinal clinic of Kings County Medical Center.

Liver function tests were performed on all patients at the start of therapy and at monthly intervals thereafter as long as they were under observation. Roentgenograms of the gallbladder and intravenous cholangiograms were obtained whenever indicated.

One of the patients with T-tube intubation of the common duct, 12 were men and 8 were women, ranging in ages from 40 to 75 years. Nineteen of these

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patients had been operated upon for common duct obstruction due to calculi, 4 for the second time. The remaining patient in this group was a male upon whom a choledocojejunial anastomosis had been performed to relieve obstruction at the lower end of the common duct. All the patients in this group showed no apparent parenchymal liver damage and the sphincter of Oddi was intact.

The bile in these 20 patients was collected at 4-hour intervals three days before and three to five days after Zanchol therapy was instituted. This was done to compare the bile before with that during Zanchol therapy for changes in color, viscosity, volume, composition of bile solids and electrolyte composition.

The technic employed for collecting the bile was that described<sup>2</sup> by Layne and Bergh. With this technic the indwelling T-tube should be as large as possible without injuring the common duct. One end of a polyethylene tubing then is inserted into the T-tube until it reaches a point near the tip of the catheter. Because gravitational force is insufficient to drain all the bile from the duct, a low constant speed suction pump attached to the catheter is utilized. When the pump is in operation the polyethylene tubing acts as a bleeder vent to prevent the duct mucosa from being pulled into the holes in the T-tube. Drainage of the common duct was considered efficient by this method if the patients' stools and gastric aspirate remained acholic while the pump was in operation.

One 250 mg. tablet of Zanchol was administered four times daily to one-half of this group and two 250 mg. tablets four times daily to the remainder. Zanchol also was compared in these patients with Decholin® (an oxidized bile acid) and Ketochol® (a mixture of oxidized bile acids) for choleretic efficacy per tablet. Results of these comparisons were determined by recording the total volume, color, viscosity and composition of bile solids in the bile collected at 4-hour intervals during the administration of each drug.

The diagnosis of noncalculous cholecystitis made in 15 patients in the present series was suggested initially by observing the typical symptoms of bloating and belching after meals as well as pain in the upper right quadrant of the abdomen which radiated into the back, shoulder and subscapular areas. In most cases the diagnosis later was established with roentgenograms utilizing single and double dye methods, which showed the gallbladder to visualize poorly and empty inadequately following a fatty meal. All patients in this group were given three 250 mg. tablets of Zanchol after each meal.

Of the four patients with a confirmed diagnosis of cholangiolitis with hepatitis, in three this condition developed secondary to treatment with chlorpromazine, and in one secondary to treatment with methyltestosterone. These patients received two to three 250 mg. tablets of Zanchol after each meal. The remaining patients received Zanchol in dosages ranging from 500 to 5,000 mg. daily, depending on the nature and progress of their disorders.

### RESULTS

The majority of intubated patients showed an increase in bile output while on Zanchol therapy, some of them as much as double the volume measured at the start of treatment. In all these patients the bile showed a marked diminution of sediment and a change in color from a muddy orange or yellow to a deep, clear green. These bile changes were associated with the finding that indwelling T-tubes remained sediment-free and unobstructed for several months without removal, thus corroborating McGowan's report<sup>3</sup> of a detergent activity of Zanchol.

In comparison with Decholin, Zanchol was shown to induce a greater total bile volume in 12 patients; an equal volume in 3 patients; and less volume in 2 patients. In comparison with Ketochol, Zanchol was shown to induce a greater total bile volume in 4 patients; an equal volume in 3 patients; and less volume in 2 patients. Measured against control periods without medication, the bilirubin content of the bile in these patients showed a diminution of from 50 to 80 per cent with Zanchol, compared with up to 50 per cent with Decholin and Ketochol.

All 15 patients diagnosed as having chronic noncalculous cholecystitis showed excellent clinical improvement and relief of symptoms. It was our impression that the 3 patients with cholangiolitis with hepatitis secondary to chlorpromazine therapy improved more rapidly with Zanchol than with other agents we had employed for this condition. The patient with cholangiolitis and hepatitis secondary to methyltestosterone therapy improved satisfactorily but more slowly than the other 3.

We believe that the clinical improvement seen in these patients and in the 5 patients with serum and viral hepatitis may have resulted from the pronounced hydrocholeretic effect of Zanchol, which acts to flush out the finer biliary radicles. It also was our impression that the patients with viral and serum hepatitis improved more rapidly when Zanchol was added to their regimen. We feel, however, that more experience with Zanchol is necessary to determine more exactly its value in this condition.

In a small number of patients the gallbladder was visualized on roentgen examination after several months of Zanchol therapy whereas it had not been visualizable before this time. This effect, however, can occur spontaneously with incomplete blockage of the cystic duct and therefore further study is required to determine if the effect was due to Zanchol.

### COMMENT

The bile plays an important role in the absorption and digestion of food by helping to emulsify fats and fat soluble nutrients as well as by activating the lipolytic and proteolytic enzymes of the intestine and pancreas. From the liver where it is excreted continuously, the bile flows into the hepatic ducts

and thence into the common duct. When its accumulation in the common duct reaches a pressure of 20 cm. of water, it is forced through the cystic duct into the gallbladder.

Here it is concentrated through a partial reabsorption of its water and water-soluble fractions, especially bicarbonates and chlorides. Normally, the bile is concentrated to from one-sixth to one-tenth that of its original volume. Cholecystic disorders such as chronic noncalculous cholecystitis with fibrosis of the gallbladder, however, will cause reabsorption of the bile acids necessary to maintain bilirubin and cholesterol in solution. This results in an overconcentration of bile which may predispose to the formation of calculi. When obstruction and stasis also are present, the bile may concentrate even more and thus further predispose to the formation of calculi.

Recurrence of symptoms, particularly biliary colic, within two to three months following cholecystectomy is termed the postcholecystectomy syndrome. Probably the most frequent cause of this syndrome is a calculus or several calculi which escaped detection in the extrahepatic ducts during cholecystectomy. Other causes include an excessively long cystic duct stump, stricture of the common duct and spasm of the sphincter of Oddi.

This spasm, termed biliary dyskinesia, also may occur when the gallbladder is intact but when the flow of bile through the ducts is impaired, due most frequently to irritation of the ducts by calculi or infection. Less frequently this spasm occurs apparently without any associated pathologic condition, and hence is termed primary or functional biliary dyskinesia.

For a short period after the gallbladder is removed by cholecystectomy or its function is eliminated spontaneously by cystic duct obstruction or chronic fibrosing cholecystitis, the sphincter of Oddi remains patent and permits the bile to trickle continuously into the duodenum. After several months, however, the sphincter of Oddi regains its normal tonus and the ducts take over the bile storing and concentrating functions of the absent gallbladder, and a normal flow of bile through the ducts into the duodenum is restored. In these circumstances, however, the common and hepatic ducts contain a concentrated bile which may predispose to stasis, obstruction and the formation of calculi.

The medical management of both chronic calculous and chronic noncalculous cholecystitis as well as the symptoms of the postcholecystectomy syndrome is directed toward increasing the flow of a clear, fluid bile and retaining bile solids in solution. Increased bile flow helps to flush out the inspissated bile from the smaller biliary radicles, while retaining the bile solids in solution prevents biliary stasis which predisposes to infection and the formation of calculi. In the present series Zanchol, a new synthetic hydrocholeretic, was shown not only to exert these activities effectively but also to have a salutary effect on the physiochemistry of the bile.

Therefore the routine use of Zanchol is indicated immediately after cholecystectomy to prevent the postcholecystectomy syndrome; in patients complaining of the symptoms of the postcholecystectomy syndrome (eructation, colicky pain, bloating after meals, backache and pyrosis) several months after cholecystectomy; and in chronic noncalculous cholecystitis with fibrosis of the gall-bladder wall.

In the diagnosis of chronic noncalculous cholecystitis, it is important to differentiate it from chronic calculous cholecystitis, to avoid a needless and often unbeneficial cholecystectomy where symptoms are not caused by the presence of calculi. This differentiation may be difficult, especially in "border-line" patients with symptoms suggesting both disorders. If the ducts appear to be unobstructed as determined by duodenal drainage, and if the inflammation appears to be due to atonicity and stasis of the gall-bladder causing impaired evacuation of the bile, a diagnosis of chronic noncalculous cholecystitis is justifiable, and appropriate medical management should be tried.

In addition to Zanchol, treatment of noncalculous cholecystitis includes a diet moderately high in emulsified fats such as are contained in egg yolk and dairy products. The ingestion of fats in these patients aids in the reduction of duodenal hypertonicity and stimulates the evacuation of bile from the gall-bladder.

A moderately high fat diet along with the administration of Zanchol also is utilized to reduce sphincter tone in functional biliary dyskinesia. We have found that the addition of an antacid or of an antispasmodic such as Pro-Banthine® to reduce gastric secretion<sup>4</sup> also is helpful in reducing duodenal and sphincter tone. Finally, personality conflicts and environmental stresses resulting in anxiety and tension may cause sphincter spasm in functional biliary dyskinesia, so that these factors should receive attention and psychotherapy be instituted if deemed necessary.

#### SUMMARY AND CONCLUSIONS

In the present study, Zanchol, a new synthetic hydrocholeretic, was given to 182 patients with various biliary disorders. Twenty of these patients were intubated after recent cholecystectomy and common duct exploration; 55 had symptoms typical of the postcholecystectomy syndrome; 90 were diagnosed as having chronic cholecystitis (75 calculous and 15 noncalculous); 3 had serum hepatitis; 2 had viral hepatitis; 8 were diagnosed as having uncomplicated cirrhosis of the liver; and 4 had a confirmed diagnosis of cholangiolitis and hepatitis. No evidence of toxicity with Zanchol was noted in these patients in doses ranging from 500 to 5,000 mg. daily for periods in some instances of more than three years.

We feel that the hydrocholeretic-detergent activities of Zanchol contributed importantly to the clinical improvement seen in a majority of patients. Hydro-

choleresis improves biliary integrity by flushing out inspissated bile from the smaller biliary radicles and preventing stasis while a detergent activity returns biliary sediment to solution adding to the fluidity of the bile and decreasing the likelihood of bile sediment deposits and calculi formation.

The effect of this detergent activity was observed in 20 intubated patients, in whom the bile changed from a muddy yellow or orange to a deep, clear green while they were receiving Zanchol. McGowan's finding<sup>3</sup> that the detergent activity kept indwelling T-tubes free from biliary sediment and obstruction was corroborated by the present study.

In comparison with Decholin and Ketochol, Zanchol was shown to reduce biliary sediment up to 30 per cent more efficiently. Although we observed good results in the small number of patients treated for cholangiolitis with hepatitis, we feel that additional experience with Zanchol is necessary to determine more exactly its value in this condition.

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## TUBELESS GASTRIC ANALYSIS IN HOSPITAL AND OUTPATIENT PRACTICE

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### INTRODUCTION

The concept of a tubeless gastric analysis is not new, and experiments along this line are amply recorded in the literature. In 1950 Segal et al described the oral use of a cation exchange resin coupled with a quinine compound which was recovered in the urine when acid was present in the stomach. This method was tedious and subject to modification by extraneous factors. In 1955 a similar technic using an exchange resin and azure A dye was introduced. This imparted a blue color to the urine if acid was present in the stomach after ingestion of the dye-resin complex. This procedure was simple, relatively quick and required no intubation. Various authors have reported accuracy ranging from 85 to 100 per cent when compared with results of gastric intubation under rigidly controlled circumstances.

It is the purpose of this study to evaluate the resin-azure A test† for gastric acidity both for accuracy and practicality as a screening procedure under more or less routine hospital and outpatient conditions.

### METHOD

On a fasting stomach each patient was given 500 mg. of caffeine sodium benzoate by mouth. One hour later a urine specimen was obtained as a control, and 2 gm. of dye-resin complex (amberlite RXE-96 plus azure A) were given. Two hours after this, a second urine specimen was obtained.

These materials are conveniently supplied by E. R. Squibb and Sons in the form of a small packet labeled Diagnex Blue Improved. This packet contains not only the necessary chemicals but also a detailed set of instructions, as listed below. The instructions for performing the test were used as printed, except that specific hours of collection, i.e. 7:30, 8:30 and 10:30 A.M. were used. Such specification of exact hours of collection was found necessary in order to avoid confusion among the nurses and among the outpatients taking the test. The directions for collecting the urine samples are as follows:

1. Do not have any part of your breakfast on the day of the test until the test has been completed.

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†Now marketed as Diagnex Blue Improved by E. R. Squibb and Sons.

2. Urinate on arising and discard this urine.
3. Open the small packet and swallow the two tablets with one glass of water.
4. One (1) hour afterwards or thereabouts, urinate and save all the urine in a jar. Put label marked "Urine Sample 1" on this jar.
5. Open large packet and pour granules into a glass of water, stir well and drink it. The granules will not dissolve—do not chew them. If any granules remain in the glass, drink them with a little more water.
6. Two (2) hours afterwards, urinate and save all of the urine in another jar. Put label marked "Urine Sample 2" on this jar.
7. Now you may eat breakfast.

Note: The urine may remain blue or green for a few days. This has no significance.

All urine specimens were processed by the author. After proper dilution to 300 c.c. the color of the second specimen was compared to known plastic color standards of 0.6 and 0.3 mg. intensity, which are supplied with the test kit. A urine darker than the 0.6 standard was judged positive for free gastric acid. Urines lighter than the 0.6 standard were acidified with one drop of 18 per cent HCl, boiled in a water bath for 10 minutes and reread after cooling 2 hours. This was done to bring out the color of conjugated dye in the urine. If the test sample was still less than the 0.6 standard but darker than the 0.3 standard, it was judged an inconclusive test. If it was less than the 0.3 standard after boiling, the patient was judged to be achlorhydric. This procedure is exactly as recommended by the Diagnex manufacturers.

All patients were subjected to intubation either before or after the Diagnex test. In some cases no stimulus was used, while in others an Ewald meal or histamine was given prior to the test.

The patients were divided into two groups. The first consisted of 11 persons on whom the test was given as an out-patient procedure. These included charity clinic patients with indications for gastric analysis and several volunteers from the intern corps and Tulane medical students who had no apparent illness. All were given the test packet with instructions to collect the urine at home and bring it to the hospital. An additional time of about ten minutes was spent with each patient going over these instructions.

The second group was composed of hospitalized patients on both private and charity wards in whom gastric analysis was desirable for routine examination or specific symptomatology. In this group the instructions were placed on the order sheet and the test administered by the ward nurse.

TABLE I

Pt. No.	Test No.	Test Vol.	Color	pH	Dilut. Nec.	Boil. Nec.	Diagnex		Intubation			Out-Patient	Corre-lation	Disease	Age	Comment
							+	±	–	Stim.	Fasting	Response				
1	1	75	B	A	–	–	None	Normal	–	–	–	–	Yes	+	None	25
2	5	150	B	A	–	–	None	Normal	–	–	–	–	Yes	+	None	25
3	10	150	B	A	–	–	None	Normal	–	–	–	–	Yes	+	Possible ulcer	26
4	11	275	L.B.	N	–	–	None	Normal	–	–	–	–	Yes	+	None	24
5	13	200	L.B.	B	–	–	None	Normal	–	–	–	–	Yes	+	None	30
6	14	125	B	A	–	–	None	Normal	–	–	–	–	Yes	+	None	25
7	15	75	B	A	–	–	None	0°	–	–	–	–	Yes	0	None	24
8	16	100	L.B.	N	–	–	None	Normal	–	–	–	–	Yes	+	None	28
9	19	100	L.B.	B	–	–	None	Normal	–	–	–	–	Yes	+	None	27
10	36	250	L.B.	A	–	–	Ewald Meal	37°	–	–	–	–	Yes	?	Questionable hemoptysis	36
11	45	60	L.B.	A	–	–	Hist.	0°	–	–	–	–	Yes	+	None found	25
12	6	200	B	A	–	–	Ewald Meal	0°	–	–	–	–	No	0	Diverticulosis	61
13	7	600	B	N	–	–	Hist.	0°	–	–	–	–	No	–	None found	27
14	9	180	L.B.	A	–	–	Hist.	31°	–	–	–	–	No	0	Active gastric ulcer	73
15	9	225	L.B.	A	–	–	Hist.	31°	–	–	–	–	No	+	Active gastric ulcer	73
16	17	500	Y	B	–	–	Hist.	0°	–	–	–	–	No	+	Prepyloric ulcer Cholangiolitic hepatitis	41
17	18	475	B	A	–	–	Hist.	0°	–	–	–	–	No	+	Active gastric ulcer	56
18	20	400	Y	A	–	–	Ewald Meal	39°	–	–	–	–	No	+	None found	62
19	22	350	L.B.	B	–	–	Hist.	20°	–	–	–	–	No	+	Active gastric ulcer	41
20	23	600	L.B.	A	–	–	Hist.	0°	–	–	–	–	No	+	Active duodenal ulcer	44
21	24	175	L.B.	B	–	–	None	13°	–	–	–	–	No	+	Hiatal hernia, diabetes	38
																Active antral ulcer

222		25	150	Y	B	V	V	-	Hist.	0°	0°	No	+	Duodenal ulcer	47
23	26	100	L.B.	B	V	±		Ewald Meal	20°		No	?	Active gastric ulcer	62	
24	27	125	L.B.	A	V	+		None	10°		No	+	Chronic pancreatitis	47	
25	28	75	B	N	V	+		Hist.	0°	67°	No	+	Active gastric ulcer	49	
														Prior intubation without histamine showed no free acid	
26	29	75	B	B	V	+		Hist.	20°		No	+	None found	54	
27	33	345	Y	B	V	+		None	40°		No	+	None found	54	
28	30	120	L.B.	B	V	±		Hist.	0°	16°	No	?	Depressive reaction	53	
29	31	340	L.B.	B	V	+		Hist.	0°	36°	No	+	Malnutrition	39	
30	32	35	B	A	V	+		Ewald Meal	0°		No	0	Menorrhagia		
31	34	170	Y	B	V	—		Hist.	0°	0°	No	+	Pernicious anemia	63	
32	35	45	Y	B	V	—		Hist.	0°	0°	No	+	Possibl spinal cord tumor	73	
33	37	75	Y	A	V	—		Hist.	0°	0°	No	+	Cholecystitis	37	
34	38	280	B	A	V	+		None	14°		No	+	Rectal stricture	82	
35	39	360	Y	A	V	V	-	None	0°		No	+	3 mos. post-op. hiatal hernia repair	54	
36	40	100	L.B.	N	V	+		Hist.	22°	99°	No	+	Recurrent symptoms after gastroduodenostomy for prepyloric ulcer	46	
37	41	155	L.B.	A	V	—		Hist.	78°		No	0	Achlorhydria on intubation 2 years ago also	57	
38	42	100	Y	N	V	—		Hist.	16°		No	0	Cellulitis of leg	63	
39	43	60	L.B.	A	V	—		Hist.	0°	0°	No	+	Mild heart failure		
40	44	180	L.B.	N	V	+		Hist.	0°	99°	No	+	Neurodermatitis	69	
														Ovarian cyst	58
														Mass in lung	62
														Ca. in situ of cervix	

## RESULTS

The results obtained in this series are illustrated in Table I. This contains all pertinent information. The volumes of the test samples of urine are given in c.c. The color of the undiluted test sample is abbreviated B., L.B. and Y. for blue, light blue and yellow. The pH of this urine is represented by A., B. and N. for acid, basic and neutral respectively. An equivocal Diagnex test is listed as  $\pm$  under Diagnex. The rest of the table is self-explanatory.

Table II compares the number of patients with false (0 correlation) or inconclusive (? correlation) Diagnex tests in each of two intubation groups; namely, the acid secretors and those with no free acid.

## COMMENT

*Accuracy:*—The Diagnex test gives only qualitative results. These, however, are the main consideration in any screening procedure for such conditions as gastric malignancy, peptic ulcer, pernicious anemia, etc., where the presence or absence of acid is the prime consideration. In such a screening test, a moderate number of false positive or inconclusive results do not negate the value of the procedure. These are merely indications for further study with intubation and are not conclusive in themselves. A false positive test, on the other hand, in an achlorhydric patient masks the pathology and prevents adequate follow-up and further examination.

In this study, as seen in Table II, there were 30 acid secretors. Of these, three or 10 per cent gave negative Diagnex tests. One of these was repeated and showed a positive test for acid on the second procedure.

In this group of acid secretors there were also three equivocal results, or about 10 per cent, in which a repeat test or intubation would have been indicated in a screening procedure.

Thus, based on these figures, in any large group being scanned by the Diagnex test, 10 per cent of the patients with gastric acid present would give negative tests and 10 per cent would give equivocal results. This means that about 20 per cent of the group with acid present would have to undergo a repeat Diagnex test or gastric intubation to determine their true status.

Of the ten patients in this series with no free gastric acid, three or 30 per cent gave false positive tests. There were no equivocal tests in this group.

On the surface, this large percentage of false positive results seems to prohibit the use of Diagnex. There are, however, several factors involved. First, the test sample is small. Second, the actual presence of achlorhydria in these three patients is open to question, since one had no stimulus during intubation and two had only Ewald meals as stimulants prior to intubation. Conceivably caffeine

sodium benzoate could be a stronger stimulant to gastric acid secretion, giving a positive Diagnex test in hypochlorhydric, instead of achlorhydric individuals. The question could have been answered simply by repeat gastric analysis using histamine; however, this was impossible in the three patients involved. In any case, no definite conclusions can be drawn on the basis of these figures alone.

It is to be noted that in the six achlorhydric patients on histamine gastric analysis there were no false positive Diagnex tests. Further studies of the accuracy of the Diagnex test are indicated. Such studies can only adequately be compared with the results obtained from intubation with histamine stimulation in the same patient. It also seems possible that histamine used as a stimulant in the Diagnex test itself would increase its accuracy but would decrease its potentiality for out-patient use.

*Practicality:*—The practicality of a test such as tubeless gastric analysis depends on three factors: 1. Ease of administration to the patient; 2. the complexity

TABLE II

	No. of Patients	Poor Correlation		
		0	?	Total
Free Acid Present	30 (75%)	3 (10%)	3 (10%)	6 (20%)
No Free Acid	10 (25%)	3 (33%)	0	3 (33%)
Total	40	6 (15%)	3 (7.5%)	9 (23%)

of laboratory procedures involved and 3. the number of contraindications to the test. Considering each one of these factors separately, there is no doubt that the administration of Diagnex is far easier than gastric intubation. Even if repetition of the procedure is required for reasons of accuracy, the tubeless method is preferred by nearly all patients. In the hospital the procedure was administered by the ward nurses with complete dependability in all 29 cases, thus freeing the interns from performing the time-consuming routine intubation. On an out-patient basis, however, some confusion existed. Four out-patient tests are not included in this study because the specimens were not collected at the proper times. Ironically enough, all four of these patients were medical students or interns who had had the usual ten-minute oral instruction plus the written directions on the test packet.

The laboratory procedure is remarkably easy if the diluted urine is positive. If the initial color is less than the 0.6 standard the tubes must be acidified, boiled ten minutes, cooled two hours and reread. This is relatively easy to do,

but from the standpoint of technician's time it is at least as complicated as titration for gastric acidity. Such further handling was found necessary in 28 or 70 per cent of the tests in this study. In addition, nine test samples were greater than 300 c.c. in volume and extra dilution of the urine was necessary before comparing with the standards.

The test is considered to be contraindicated in such conditions as severe liver disease, congestive heart failure, severe renal disease, malabsorption syndromes, pyloric obstruction and obstructive urinary tract disease. The test is of doubtful value in these conditions because of its effect on dye absorption and excretion. A recent study by Rodman, Gutman and Myerson indicates that actually only severe liver and renal disease tend to modify the results. From the standpoint of toxicity of the dye-resin complex the test is remarkably safe. No side-effects or abnormal reactions were encountered in this study or are reported in any of the literature.

#### SUMMARY

1. A method of tubeless gastric analysis using a cation exchange resin combined with azore A dye is compared in 40 patients with the results obtained from gastric intubation.

2. The accuracy of the test is discussed but no definite statistical conclusion can be drawn from this study. Unless, however, further investigation proves the procedure to be more reliable than indicated here, it is my opinion that it *cannot* replace intubation in routine hospital and out-patient practice. The use of histamine as a stimulus instead of caffeine sodium benzoate will probably make the test more dependable.

3. The test is easily administered and has few contraindications but requires as much, if not more, laboratory procedure as titration of gastric secretion.

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## DISCUSSION

*Dr. Murrel H. Kaplan (New Orleans, La.):*—The question has been raised over the past few years as to the applicability of tubeless gastric analysis as a screening test in hospital and out-patient practice in replacing the time honored intubation. The latter is uncomfortable for the patient and is time consuming for the intern whose services are felt to be more valuable in other capacities.

The answer has been given you. The tubeless gastric analysis may well find a place in massive screening of asymptomatic individuals to evaluate the necessity for upper gastrointestinal series in those who are achlorhydric, but the percentage of false negative, and more important the percentage of false positives, precludes its use at this time in routine hospital and outpatient practice.

A recent article by Denborough et al of England<sup>1</sup>, investigating 124 patients arrived at a similar conclusion.

Dr. Sternberg is to be complimented on his paper. In spite of the many demands for his services, he has been able to record some observations which have practical application in clinical gastroenterology.

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## A BALLOON-KYMOGRAPHIC STUDY OF THE EFFECTS OF TRICYCLAMOL ON COLONIC MOTILITY IN IRRITABLE COLON\*

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In a previous study tricyclamol was shown to inhibit the motility of the stomach and the small intestine<sup>1</sup>. Since hypermotility is frequently present in irritable colon it was decided to investigate the effect of the drug on the motility of the colon in patients with this condition. This paper is a report of these studies in which the balloon-kymographic method was employed.

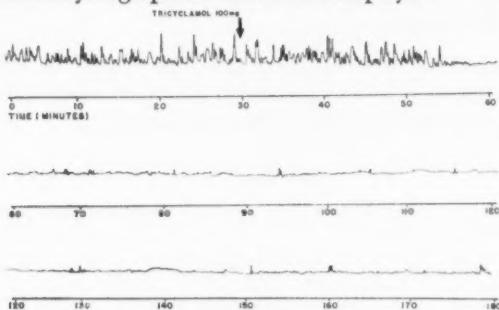


Fig. 1

### METHOD

Forty-two ambulatory patients were used in this study. The patients fasted for 12 hours, and on the morning of the experiment, the bowel was cleansed with three tap water enemas. Under sigmoidoscopic guidance a balloon was inserted into the sigmoid, inflated with 30 c.c. of air, and connected through a water manometer with a kymograph. After a control tracing of 30 minutes' duration, 100 mg. of tricyclamol was given by mouth. In most cases the tracing was continued for another 120 minutes. In one case in which anticholinergic activity appeared to be unusually prolonged, the tracing was continued for 3 hours.

The effectiveness of tricyclamol in reducing colonic motility was expressed as positive if there was a cessation of spontaneous contractions of more than 30 minutes' duration, indeterminate if the cessation was less than 30 minutes, and negative if no effect on contractions was observed.

\*From the Lenox Hill Hospital, New York, N. Y.

These studies were supported and tricyclamol supplied by Burroughs Wellcome & Co. (U.S.A.), Inc.

## RESULTS

Seventeen patients were excluded from this study. Lack of cooperation was the most common cause of failure to complete the experiment. In 4 of these patients there was little evidence of colonic motility for 30 minutes after the balloon was inserted and the procedure itself appeared to inhibit contractions. In 11 of the remaining 25 patients the results were positive, the duration of the inhibitory effect varying from 30 minutes to 2 hours. The average time between

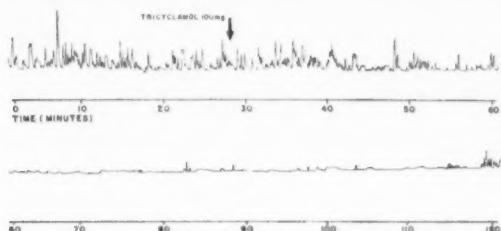


Fig. 2

the administration of the drug and a demonstrable effect on motility was 25 minutes. In 7 patients the results were indeterminate. In these cases a definite effect on motility was noted, but the suppression of contractions lasted less than 30 minutes. In some instances the contractions ceased for variably short periods, resumed activity for 3 or 4 minutes and then ceased again. In 7 patients tricyclamol failed to influence the motility of the colon.

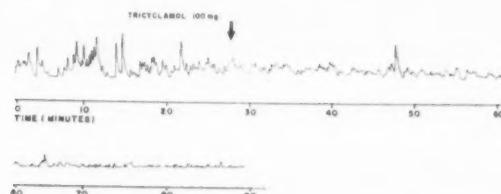


Fig. 3

## COMMENT

Our results indicate that tricyclamol, by decreasing the frequency and amplitude of contractions, has a distinct antispasmodic action on the colon. Its previously shown suppressive effect on the motility of the stomach and small intestines suggested a similar action on the colon, though drugs that affect the motility of the stomach are known to have a less pronounced effect on the colon<sup>2</sup>.

In our experiments 100 mg. tricyclamol orally diminished motility in 18 out of 25 patients. The duration of antispasmodic action varied from case to case.

Thus in A.R. (Fig. 1) inhibition of contractions lasted more than 2 hours, while in case A.M. (Fig. 2), R.A. (Fig. 3), and G.D. (Fig. 4), the inhibition of contractions while definite were not so prolonged. In certain instances, as in L.R. (Fig. 5) the drug had a short suppressive effect; an indefinite effect, as in J.B. (Fig. 6); or no effect as in D.J. (Fig. 7).

The fact that tricyclamol does not diminish contractions in all cases of irritable colon suggests an explanation for some of the failures of anticholinergic drugs in relieving cramps and diarrhea. These symptoms may be either due to

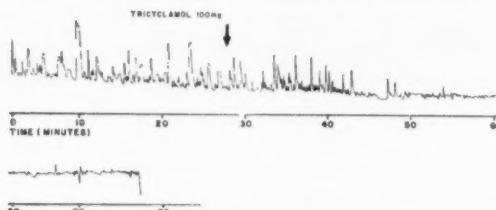


Fig. 4

hypermotility, an exaggeration of normal motility, or to dyssynergia, an abnormal type of motility. Anticholinergic drugs have no effect on abnormal motility<sup>3</sup>.

In using anticholinergic drugs it might be of value to keep in mind just what effects we are trying to produce. As Posey<sup>4</sup> has pointed out, "What would be the net result in the human being if these preparations succeeded in accomplishing a full antispasmodic effect when given by mouth? Quite obviously functional paralytic ileus would be produced. The intestines would be both atonic and nonmobile, in effect, paralyzed. Such a state is no more normal or desirable than the supposed hypermotility and spasm which occasion the use of these drugs".

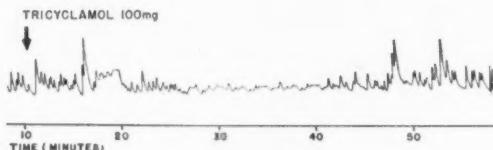


Fig. 5

#### SIDE-EFFECTS

Twenty patients complained of dryness of the mouth. Two patients had transient blurring of vision. Because double the recommended therapeutic dose of tricyclamol was employed in these experiments it was expected that this evidence of anticholinergic action would be encountered.

Colonic nerve impulses, received by the sphincter muscle of the iris, ciliary muscle of the lens, and the cells of the salivary glands, are identical with those

received by the muscle cells of the colon. A potent anticholinergic drug will, therefore, affect all these structures, and inevitably give rise to some side reactions. It appears impossible with the drugs available at present, to obtain therapeutic responses without some side-effects. Indeed, Almy<sup>5</sup> found that drugs without side-effects were also without desirable effects on the colon. Then again, side-effects may serve a useful purpose, for dryness of the mouth is often the only indication that anticholinergic effects are being obtained. It would appear,

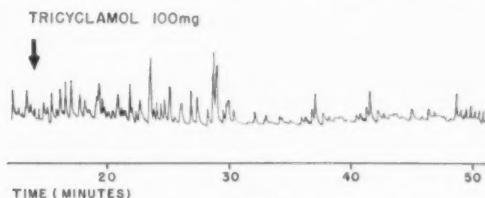


Fig. 6

however, that not all anticholinergic drugs affect the eyes and the salivary glands to the same degree. Thus, tricyclamol in the treatment of peptic ulcer produced definite anticholinergic effects with slight side-effects<sup>1</sup>. The fact that individual drugs appear to have a selective action on different parts of the body innervated by the cholinergic nerves gives rise to the hope that the synthesis of compounds having greater specificity of action on these structures will soon be accomplished<sup>6</sup>.

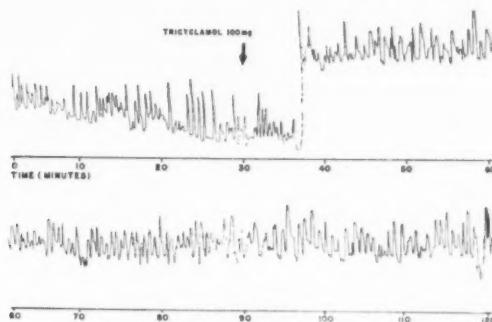


Fig. 7

#### SUMMARY AND CONCLUSIONS

The effect of 100 mg. of orally administered tricyclamol on colonic motility was studied in 42 patients by means of the balloon-kymographic method. Observations were completed on 25 patients. The average time between administration of the drug and the effect on motility was 25 minutes. In 11 patients motility was suppressed for periods varying from 30 minutes to 2 hours. In 7

patients there was inhibition of motility for periods of less than 30 minutes. In 7 patients tricyclamol had no effect on motility.

Because of its inhibitory effect on colonic motility in some cases of irritable colon it is suggested that tricyclamol may prove useful as an adjunct in the treatment of this disease.

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## CLINICAL EVALUATION OF AN ANTICHOLINERGIC IN THE IRRITABLE COLON SYNDROME\*

### A DOUBLE BLIND STUDY OF TRICYCLAMOL

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The primary etiologic factors in the irritable colon syndrome are emotional conflict and tension. The emotional disturbance may be due to many causes, but is usually associated with resentment, fear, and guilt<sup>1</sup>. The colonic symptoms characteristic of irritable colon are due to overstimulation of the parasympathetic nervous system. The exact manner in which this occurs is not clear, but there is evidence that the action is through the hypothalamus<sup>2</sup>.

In the treatment of this condition, antispasmodics have always been extensively used. Even though "spasm" is often illusory, the popularity of these drugs has not been lessened. Many of the common antispasmodic drugs taken orally in nontoxic doses, however, have little or no demonstrable effect on colonic motility, and in recent years the newer anticholinergic drugs have been extensively employed<sup>3,4,5</sup>.

Balloon-kymographic studies in normal subjects and in subjects under artificial stress<sup>6</sup> have shown that a number of new anticholinergic drugs are capable of suppressing colonic contractions. One of these agents, tricyclamol, has been effective in inhibiting contractions of the stomach and small intestines<sup>7</sup> as well as the colon<sup>8</sup>. It was decided, therefore, to study the effect of this drug in irritable colon in comparison to the effects of phenobarbital and a placebo.

In a study of this type several problems arise. Where psychosomatic influences are prominent the problem of evaluating a new agent or treatment is always difficult. Spontaneous remissions and exacerbations may in large part be determined by environmental conditions regardless of therapy. Suggestion must be avoided. The fact that a new drug is being used must not be emphasized. In the irritable colon syndrome as in peptic ulcer a new drug enthusiastically prescribed by the physician will frequently produce temporary improvement.

### METHOD OF STUDY

To make the study as objective as possible, it was decided to employ the double blind method, the nature of the preparation being unknown either to us

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or to the patients. We were furnished with four identical tablets the contents of which were disclosed by the manufacturer at the end of the study. Tablet L contained 50 mg. of tricyclamol; tablet E 50 mg. of tricyclamol and 16 mg. of phenobarbital. Tablet R contained 16 mg. of phenobarbital, while tablet H was a placebo.

*Material and procedure:*—Seventy-seven patients with irritable colon from the out-patient department, private patients in the hospital, and patients in private practice were used. The patients were divided into four groups: Group I received tablet L; Group II tablet E; Group III tablet R; and Group IV tablet H. In each case the diagnosis of irritable colon was established on the basis of history, and on the exclusion of organic disease by physical, roentgen, sigmoidoscopic, and laboratory examinations. All patients were maintained on a bland diet. No medication other than the preparations under study were prescribed, and care was taken to give the patients no reassurance or other psychotherapy. To diminish the effect of suggestion the patients were told nothing

TABLE I  
RESULTS OF DOUBLE BLIND STUDY IN 77 PATIENTS WITH IRRITABLE COLON

Group	Drug	No. Pts.	Improved	Unchanged	Worse	Not Followed
I	Tricyclamol	20	7	4	7	2
II	Tricyclamol & Phenobarbital	19	11	2	4	2
III	Phenobarbital	19	10	4	5	
IV	Placebo	19	9	1	8	1

about the drug, but were asked to take one tablet four times a day and to note what effect it produced on symptoms. On return visits the patients were questioned as to the presence of epigastric distress, cramps and flatulence, borborygmi, and the number and consistency of stools. At the end of the 30-day period (or sooner if the preparation was discontinued) the symptomatic response was evaluated, the results being recorded as improved, unchanged, or worse. In most cases patients showing no improvement at the end of two weeks discontinued the medication. Those who felt they had improved were allowed to continue the agent as long as they desired (Table I).

#### RESULTS

*Group I:*—Tablet L; 50 mg. of tricyclamol. Twenty patients received tricyclamol alone. The duration of treatment varied from two weeks to 14 months. Seven patients claimed they felt better, seven felt worse, and four noted no change. Two patients took the drug for only three days.

It was noted in this group that the effects of anticholinergic therapy are readily apparent. If no improvement occurs in the first week none will likely occur no matter how long the preparation is taken. Similarly, if improvement occurs it is rapid.

**Group II:**—Tablet E; 50 mg. of tricyclamol and 16 mg. of phenobarbital. Nineteen patients were treated with tricyclamol and phenobarbital. The duration of treatment was from five weeks to 18 months. Eleven patients stated that they were improved, four felt worse, and two noted no change. Two patients discontinued the medication after three days.

**Group III:**—Tablet R; Phenobarbital 16 mg. Nineteen patients received phenobarbital. Ten patients were improved, five felt worse, and four noted no

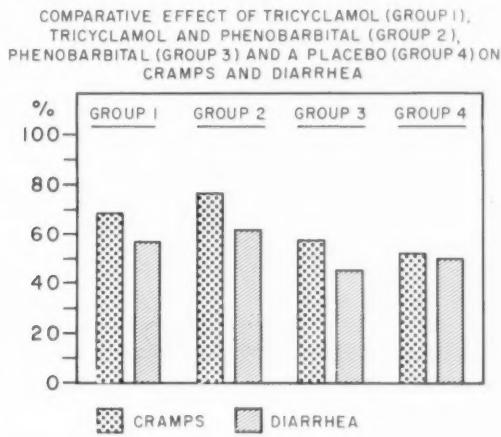


Fig. 1

change. One patient stopped taking the medication after six days. The duration of treatment was from four weeks to eight months.

**Group IV:**—Tablet H; Placebo. Nineteen patients were treated with a placebo. The duration of treatment lasted from one month to three months. Nine of this group stated that they were improved, one noted no change, and eight stated they felt worse. One of the patients stopped the medication after four days (Fig. 1).

#### COMMENT

The symptomatic evaluation of an anticholinergic drug in irritable colon can be approached from two points of view: the effect of the drug on individual symptoms and its effect on the patient's feeling of well-being. The two do not necessarily go hand in hand. Thus of 20 patients who took only tricyclamol, 15

noted varying degrees of improvement in diarrhea. In six of these the diarrhea had practically ceased. Yet surprisingly some of these patients who had impressive relief of this most annoying symptom, stated that the drug either produced no significant change or else made them feel worse. The reason for this is that the anticholinergic drug has no effect on tension, which is the basis of the patient's complaints. The emotional problems besetting the patient remain unchanged. Another reason is that symptoms in irritable colon change rapidly and what is bothering the patient intensely one day, may be unnoticed the next. Furthermore, some patients become so preoccupied with side-effects such as dryness of the mouth that they tend to ignore the apparent beneficial effects of the drug.

Tricyclamol in the dosage used produced decided anticholinergic effects with clinical evidence of diminished intestinal tone and motility. Since this was

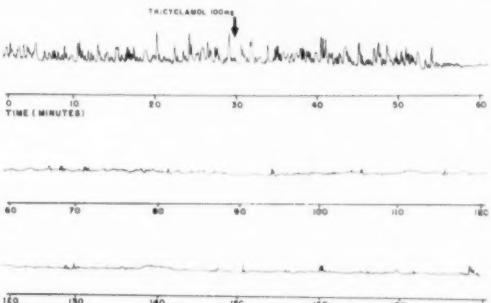


Fig. 2—Prolonged suppression of colonic motility by 100 mg. Tricyclamol by mouth.

seen in several instances in which the over all result was unsatisfactory to the patient it would appear that motor activity of the bowel plays a minor part in the symptoms of irritable colon. This was well illustrated in one patient who stated he felt worse after taking tricyclamol but who, during kymographic study, demonstrated an impressive suppression of colonic motility for more than two hours (Fig. 2).

Tricyclamol and tricyclamol with phenobarbital appeared to have a favorable effect on cramps and diarrhea. As far as these symptoms are concerned, tricyclamol especially when combined with phenobarbital, was superior to phenobarbital alone or to the placebo. Phenobarbital decreased tension and while the patients stated they felt better, in most cases somatic symptoms did not improve as much as the mental state. Nevertheless, the good results obtained with phenobarbital and especially with the placebo raise doubt as to the value of anticholinergic drugs in irritable colon. These patients are often under great stress. The gastrointestinal tract may respond to stress either through the autonomic pathways involving the postganglionic nerve endings of the target organ,

or through the coordinating centers of the brain, the pituitary and the adrenals. When hypermotility is due to cerebral excitation rather than to peripheral influences, phenobarbital which acts upon the cortex is frequently more effective than anticholinergic drugs. This is not surprising since phenobarbital lessens the individual's receptiveness to noxious stimuli from his environment. An anticholinergic merely blocks to a degree the response of stimuli directed toward the peripheral organs and numerous other responses mediated by other fibers such as the adrenergic fibers. The results obtained with the placebo are not surprising since Wolf has shown they may produce not only extensive effects simulating those of pharmacologically active drugs, but toxic effects as well<sup>9</sup>.

We have found that the presenting symptoms emphasized by the patient are often of little importance in treatment. In most cases the real trouble is one of psychic origin and the major role is played by a neurosis. Patients in whom symptoms are a result of a severe neurosis usually obtained the poorest results with tricyclamol. Grace<sup>10</sup> has noted that anticholinergic drugs affect the colon only when the emotional condition of the patient is quiet and the anxiety not severe. The routine use of anticholinergic and antispasmodic drugs in patients with irritable colon without regard to their emotional problems is inadequate therapy. Putting the colon at rest is important, but it is only a part of the treatment. The physician should also help the patient to understand the cause and effect relationship of the day-to-day stress factors of his complaints. While the average physician has neither the time nor the experience to undertake extensive psychotherapy (nor is it frequently necessary), simple explanation and reassurance often produce gratifying results. This is especially true when the psychic factors are of recent origin and not of a recurring nature. The more severe neurosis must be left to treatment by the psychiatrist. Dependence upon drugs to the exclusion of other means of treatment will fail to bring maximum benefits to the patient.

#### SUMMARY

The effects of tricyclamol, tricyclamol with phenobarbital, phenobarbital, and a placebo, were studied in patients with irritable colon by the double blind method. The average duration of treatment was one month. The patients were asked to note the effect on gastric distress, bloatedness, borborygmi, cramps, and diarrhea. At the end of the period the patients noted whether they felt better, the same, or worse.

Of the four preparations, tricyclamol when combined with phenobarbital, appeared to give the best results. It appeared noticeably more effective than tricyclamol or phenobarbital alone. All three of these preparations produced decrease in cramps and diarrhea. With phenobarbital alone or with the placebo, the effects on tone motility were less evident but almost as many patients felt better as when an anticholinergic drug was used. The result would indicate that anticholinergics *per se* are not of great value in irritable colon.

In spite of the fact that tricyclamol has a significant effect on tone and motility, as shown by decrease in cramps and diarrhea, the relief of these symptoms did not always produce over all clinical improvement. Some patients in whom amelioration of symptoms occurred claimed that on the whole they felt no better. This would appear to confirm the fact that psychiatric factors play a major role in many cases of irritable colon.

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## GASTROINTESTINAL HEMORRHAGE DUE TO TYPHOID FEVER

### REPORT OF A CASE WITH AUTOPSY FINDINGS

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The incidence of typhoid fever in the United States has decreased from 27,201 cases in 1930<sup>1</sup> to 1759 in 1955<sup>2</sup>. The disease has become somewhat rare, and although an internist may see an occasional case, only the older clinicians have had any extensive experience with it and its complications. There were approximately 1½ million people visiting foreign countries in 1957, and of those ½ million visited Mexico<sup>3</sup> where there are approximately 50,000 cases of typhoid fever per year. Thus, with transportation making epidemic and endemic areas more readily accessible to the traveler, typhoid fever must still be considered in the differential diagnosis of unexplained systemic infection, especially in people who have recently visited doubtful areas.

We would like to report a case record of a 22-year old woman who was admitted to the Second Medical Division of Kings County Hospital as a result of having severe gastrointestinal hemorrhages which were caused by typhoid fever. She had recently left an area endemic for typhoid fever in Mexico. We have reviewed the literature written in English and some of the foreign literature concerning this complication of typhoid fever.

#### CASE REPORT

This was the first Kings County Hospital admission of a 22-year old single, white American female who entered on 2 October 1957, with the chief complaint of rectal bleeding of 7 hours' duration, nausea, diarrhea, and fever of 14 days' duration. The patient had never been out of the New York area until she visited Mexico in July, August, and the first week of September. The past history and family history were unimportant. She had not been vaccinated against typhoid fever. She remained in the vicinity of Mexico City but did visit some of the nearby villages. She returned home on 7 September 1957, in good health, and on 21 September she felt dizzy and had a headache, but attended a wedding that same evening. Two days later she felt "sleepy", noted blurred vision and a

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Dr. Harold Cottle of the Department of Pathology made available the pathological material.

sore throat. Her private physician made the diagnosis of upper respiratory infection. She was sent to bed and then began to develop anorexia, nausea and constipation. She was seen again by her private physician who, on 25 September, treated her with tetracycline for two days for an "ear infection", at which time her temperature was 103° F. She also had "gas pains" in her epigastrum and suprapubic areas radiating to the entire abdomen. She was last seen by her private physician on 27 September, and was said to be somewhat improved, but was given an injection of penicillin and one cortisone tablet per day for three days, presumably for nonspecific aching in her fingers and wrists. She continued experiencing the same symptoms with nightly fevers to 103° F. Her abdominal pain increased, and in the early morning of 22 October, she developed watery diarrhea with abdominal cramps. She went to the bathroom and noted red blood coming from her rectum. She fainted in the bathroom, and was brought to Kings County Hospital.

On admission the patient appeared anxious and in moderately acute distress. Her vital signs revealed a temperature of 104° F., pulse rate of 70 per minute, blood pressure of 100/52, and respirations of 22 per minute. The only positive physical findings were: Slight diffuse tenderness on abdominal examination and hyperactive bowel sounds. Rectal examination revealed bright red blood on the examining finger. Laboratory studies showed a hemoglobin of 8 gm., a white blood-cell count of 3,700/ cu. mm., with 81 per cent lymphocytes, 6 per cent monocytes, and 13 per cent polymorphonuclear cells. The urine had a specific gravity of 1.024, a trace of protein, a moderate amount of acetone, and in the urinary sediment 20 red blood cells per high-powered field were noted. Tests for blood coagulation were normal. Sigmoidoscopy to 25 cm. showed a normal mucosa and it appeared that blood was coming from an area above the limits of the sigmoidoscope.

*Clinical course:—*The patient continued to lose blood per rectum with an estimated loss of about 3,500 c.c. and was transfused with seven pints of blood in 12 hours. She was started on chloramphenicol 1 gram by mouth and 1 gram intramuscularly 2 hours later. Her pulse rose gradually and respirations increased, and she died suddenly at 2 a.m. *Salmonella typhi* was recovered in cultures of her blood and urine.

#### AUTOPSY FINDINGS

The body was that of a well developed, well nourished young white female adult. There was an estimated 200 c.c. of yellow clear fluid in each pleural space. The heart was not remarkable and showed only microscopic cloudy swelling with some loss of sharpness of the cross striations of muscle fibers. The lungs showed pulmonary edema and congestion of moderate degree. The spleen was enlarged, weighed 480 gm., and the capsule was tense. The pulp was mushy and dark red with obscured follicular markings. Microscopically there was marked

congestion with many large monocytic cells in the sinusoids and in the center of some follicles there were foci of inflammation and necrosis. The liver weighed 1,370 gm. and was edematous and congested with microscopic foci of mono-nuclear periportal infiltration and sublobular necrosis. Colon and small intestine manifested severe lymphoid hyperplasia with overlying hemorrhagic ulcerations. The mesenteric lymph nodes were markedly enlarged and showed a pronounced reticulum-cell hyperplasia, many large monocytic cells, and central follicular necrosis. The bone marrow showed microscopic foci of necrosis. An unusual finding was the lymphoid hyperplasia of the thyroid with many macrophages, and necrosis in the germinal centers. Postmortem cultures taken from the blood, mucosal scrapings, stools, lymph nodes and spleen were all positive for *Salmonella typhi*.



Fig. 1—Representative area in the ileum showing three small ulcers.

#### COMMENT

Callendar and Luippold<sup>4</sup> showed that in persons exposed to a common contaminated water supply, the incidence of typhoid fever among the non-immunized group was 7 per cent compared to an incidence of 1.1 per cent in the vaccinated group. Duncan<sup>5</sup>, in reporting an outbreak of typhoid fever from contaminated orange juice, found that those not inoculated had 25 times greater incidence of the disease than did inoculated persons. On the other hand, Jordan and Everly-Jones<sup>6</sup> reported that 80 of 239 British soldiers who developed typhoid fever had received three yearly typhoid vaccinations and their disease was just as severe as those not receiving vaccinations. These are representative of many reported studies which illustrate the same point, namely that typhoid vaccine, while not completely protective, markedly decreases the chances of

contracting the disease on exposure. These results further suggest that the protection conferred by the vaccine is only relative, since the infectious dose may be very large, as in the cases of Jordan and Everly-Jones, and the immune mechanism may be overcome. Thus, Kean<sup>3</sup>, quoting the U.S. Public Health Service, recommends that all travelers to foreign countries should receive typhoid vaccine.

The incidence of intestinal hemorrhage in typhoid fever reported by different authors varies from 0.29<sup>7</sup> to 73<sup>1</sup> per cent. This discrepancy may be due to different standards in criteria for the diagnosis of intestinal hemorrhage. Stuart and Pullen<sup>1</sup> state that 21.1 per cent of their 360 cases had gross blood in their stools and 52 per cent of the remainder had chemical evidence of blood in their stool. The amount of blood lost is usually not excessive and rarely necessitates transfusion. There have been reports of blood loss as high as 2,500 c.c.<sup>8</sup>, but this is not common and an estimated loss, as in this patient, of 3,500 c.c. is most unusual. Hemorrhage may occur as early as the seventh day and as late as the sixtieth day<sup>9</sup> but occurs most commonly at the end of the second week and in the third week of illness. As there is no extensive loss of mucosa and opening of large vessels before the second week, these earlier hemorrhages are said to occur from the soft spongy and exceedingly hyperemic Peyer's patches which are located in the terminal three feet of the ileum and ascending colon. The later hemorrhages are due to loss of mucosa from involvement of Peyer's patches and solitary follicles. Very late hemorrhages are thought to be due to imperfectly thrombosed vessels in the floor of ulcers even when intestinal lesions tend to be healed<sup>10</sup>. The onset of hemorrhage is rarely heralded by symptoms and is usually not accompanied by pain, and may occur when the patient is improving. It has also been reported as occurring after chloramphenicol therapy has been instituted<sup>11</sup>. Stuart and Pullen<sup>1</sup> found that intestinal hemorrhage occurred in all but one of their patients who perforated, and 26 of their 76 cases who suffered the loss of grossly visible blood eventually expired.

#### SUMMARY

The case record of a 22-year old woman who died as the result of severe hemorrhages, and despite transfusions, in the third week of typhoid fever which she contracted in Mexico, has been presented and discussed.

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## ULCEROGENIC TUMOR OF PANCREAS

### CASE REPORT

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In 1955 Zollinger and Ellison described the syndrome of the ulcerogenic tumor of the pancreas<sup>1</sup>.

The cardinal features are:

1. Peptic ulcers resistant to conventional medical and surgical therapy.
2. Extraordinarily high and sustained gastric acid secretions, persisting after the antral and cephalic secretory pathways have been removed.
3. Multiplicity and often atypical location of ulcerations in the second and third part of duodenum and upper jejunum.
4. The presence of a pancreatic islet cell tumor, removal of which (when feasible), may result in disappearance of ulcerogenic tendency.

Ellison has reported 24 cases, 19 of which were due to malignant adenoma. It occurred most often in fourth and fifth decade of life and was most common in the female<sup>2</sup>.

### CASE REPORT

A 37-year old white male was first admitted to Santa Barbara Cottage Hospital, 4 November 1954, complaining of nausea, vomiting and epigastric pain of 4-hour duration.

Past history revealed that he had diarrhea, consisting of 2 to 4 watery stools per day for 14 years and had lost 20 lbs. in weight. In February 1954, he experienced a severe epigastric pain of 15 minutes' duration. In July 1954, following a similar attack, a laparotomy was performed in another hospital and numerous adhesions about the jejunum and transverse colon were found. In October 1954 gastroscopic examination revealed enormous rugal folds throughout the body of the stomach. Physical examination revealed a tender abdomen. The white blood count was 24,600 with a shift to the left. The urinalysis, icterus index, total serum protein and A/G ratio, VDRL and BSP, and glucose tolerance test were within normal limits. Gastric analysis demonstrated 7 degrees free HCl and 23 degrees total HCl fasting, after histamine injection 106 degrees of free HCl and 117 total HCl were obtained. Gastrointestinal x-rays showed large

coarse gastric rugae and a "deficiency pattern" in the jejunum. (In retrospect upon studying these films at least one jejunal ulcer was present.) The patient improved on symptomatic treatment and was discharged in 13 days.

In February 1955, the patient was readmitted for trial of steroid therapy as a sprue-type diet, vitamins, and anticholinergic drugs had been of no benefit on his diarrhea. Urinalysis, NPN, blood sugar, total serum protein, van den Bergh, serum sodium, serum potassium, serum chloride, serum potassium CO<sub>2</sub> combining power and alkaline phosphatase, were normal. A fasting gastric analysis showed 11 degrees free HCl and 14 degrees total HCl. Stool examination showed 4 plus fatty acid crystals.

ACTH and then cortisone were administered from 8 February to 2 April 1955. Two days after starting the steroids he had a formed stool for the first time

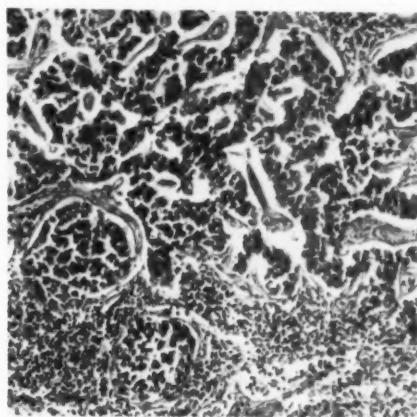


Fig. 1—The margin of the islet cell tumor within the lymph node. Clusters of islet cells are here proliferating within dilated central sinusoids of the lymph node. (x 600)

since 1950 and felt much stronger. Gastrointestinal x-rays showed considerable improvement in the "deficiency pattern" of the small bowel.

The third admission was January 1956, following three days of gaseous distention and abdominal cramps. White blood count was 16,800, urinalysis, urine bile, porphyrin, serum lipase and amylase, were normal. A provisional diagnosis of partial bowel obstruction was made and a laparotomy was performed. A partial jejunal obstruction resulting from adhesions was found. The subjacent lymph nodes were enlarged. An anterior gastrojejunostomy was performed and he was discharged 19 days later.

The patient was admitted on 16 February 1956 for the final time because of back pain. He improved on symptomatic care until 28 February 1956 when severe abdominal pain, radiating to the back, commenced. The following morn-

ing he was in shock, with marked abdominal distention and tenderness. Later that day, hematemesis and melena commenced. Fluid aspirated from the peritoneal cavity contained an amylase of 8,000 Somogi units. Despite supportive care and whole blood transfusions, he died the following day, 1 March 1956.

*Autopsy*—Significant autopsy findings included a perforated marginal ulcer of the jejunum, massive chemical peritonitis, giant hypertrophic rugae of the stomach and five penetrating ulcers, 12 to 32 mm. in diameter in the proximal jejunum, between the ligament of Treitz and the gastroenterostomy. The pancreas was of normal size and configuration and showed no evidence of pancreatitis. The gland was sectioned transversely at 3 mm. intervals and no discrete nodules were found. The lymph nodes about the pancreas, in the *parta hepatis* and in the proximal half of the mesentery were enlarged, discrete and soft.

The most pertinent microscopic finding was encountered in a lymph node adjacent to the pancreas. One half of this node was replaced by an infiltrating neoplasm, measuring 8 x 5 mm. composed of polyhedral to squat columnar cells 15 to 20 microns in diameter. In some areas these cells formed alveolar clusters and in other areas distinct tubule formation was present. With the periodic acid Schiff, Gomori trichrome stain and the Nerenberg modification of Gomori's islet stain, no cytoplasmic granules were demonstrated. The tissue block was sent to Dr. G. Gomori for special staining and he commented that the cell type could not be identified because no stainable granules were present but there was no doubt about the islet cell nature of the tumor<sup>2</sup>.

#### COMMENT

The autopsy findings of multiple peptic jejunal ulcerations with their complications of adhesion formation, partial obstruction, hemorrhage and perforation, explain the perplexing clinical course. Chronic diarrhea associated with an abnormal small bowel roentgenographic pattern was seen also in one of the cases reported by Zollinger and Ellison<sup>1</sup>. Although the islet cell tumor within the peripancreatic lymph node was probably a metastasis, an exhaustive search for the primary lesion was fruitless. The pancreas was examined sufficiently to eliminate it as a primary site. A careful search for a primary in heterotopic location was of no avail, although the tumor was unmistakably of islet cell origin.

Poth states that experimentally the relationship of pancreatic function and peptic ulcer formation has been noted for many years. When the exocrine secretion of pancreas is removed from the duodenum with the gland left intact, peptic ulcers develop spontaneously. When the duodenum is deprived of pancreatic secretions by pancreatectomy, ulcerations rarely develop<sup>4</sup>.

This led to the postulate that a hormonal factor not yet discovered, acting on the gastric mucosa directly, may be the cause of peptic ulcerations. That this

hormone is secreted by the islet cell tumor is borne out by observation of Ellison with the return of gastric secretions to normal limits following resection of a non-insulin producing islet cell tumor of the pancreas in a patient with recurrent marginal ulcerations.

In view of the usual adverse effect which cortisone may have on peptic ulceration, the clinical and radiographic improvement which the patient experienced during ACTH and cortisone therapy is worthy of special emphasis.

Examination of the pancreas should be included in all patients operated on for peptic ulcer, especially those individuals with atypical or recurrent ulcerations. Ellison also suggests that not only should the surgical procedure include removal of the pancreatic tumor combined with a standard ulcer procedure but in view of the difficulty in palpation of the small pancreatic adenoma, consideration should be given to resection of the body and tail of pancreas before resorting to total gastrectomy to control gastric acidity<sup>3</sup>.

#### SUMMARY

A patient with a clinical syndrome of chronic diarrhea, recurrent episodes of abdominal pain, gastric hyperacidity and giant hypertrophic gastric rugae was found at autopsy to have multiple peptic jejunal ulcers, one of which had perforated. A microscopic finding was the presence of an islet cell carcinoma.

This is considered an example of the Zollinger-Ellison syndrome (ulcerogenic tumor of the pancreas).

The observation of improvement, clinically and radiographic while receiving cortisone is recorded.

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## EDITORIAL

### WHY WE ARE HERE!

The American College of Gastroenterology came into existence at about the beginning of fear and doubt in the world. The suggestions at that time were that gastroenterologists owed a service to the medical profession which was not being met. The clamor for better diagnostic and therapeutic work in the abdomen throughout the medical profession was loud and strong. There was a rationale for this in that the profession was handicapped in opportunities or places to acquire knowledge in the medical abdominal field; shortage of scholars who had the ability to create notable ideas; bold new concepts were practically missing. The need for such places and persons was desperate. In this country opportunities for teaching gastroenterology had been missed. While ambition and healthy attributes were present, there was no place or way to put these into operation for better knowledge. It has always been the custom and a major need that the profession of medicine keeps teaching itself. This was not being met because there were too few teachers and practically no organizations and places to get such education. One of the major needs was for education and yet there was present no desire to develop education. We were a progressive, loyal and generous people, and a demand existed on the part of the profession for better quality of work, and our organization was established to help accomplish this. In this service, this organization has always been prominent, which is the source of its past strength, and this is reflected in its future plans.

Perhaps the most important service that an organization can perform is to be itself. We had an educational mission to fulfill and in this we take pride in the courage and resourcefulness of trying new ventures and approaches and pioneering in the spread of worthwhile knowledge throughout the profession. We are proud of this record.

It was the desire of the founders of the organization to be responsive to the needs and interests in the necessity for better abdominal work in the nation. It was felt that its institution in the City of New York, where the profession is large, would give it a good start. The small group that organized it, has now spread to a "community at large", including all of the nation and places abroad. The small group were teachers in a medical college, the New York Polyclinic Medical School and Hospital. Recognizing as they did the necessity of better gastroenterological work throughout the nation, the place of its origin and men naturally took on an educational atmosphere. They did not want to establish another of the old style specialty organizations that interested only a limited number of men. They wanted to broaden the subject so that the profession and the public would be benefited by its activities. The word "service" should be understood in this context, and its philosophy is reflected in the organization's attempts to render broader service. Programs to extend our educational offerings

reached down to the general practitioner as well as to all interested. Provisions were made for all classes of physicians to join and engage in the program and activity. They recognized the fact that while gastroenterology was an important study, worthy of special study, it was still part of internal medicine. To bring all this about the organization maintains a special program and conducts a teaching seminar each year at the time of the annual convention. These are conducted by able men, many of them from the hospitals and colleges in the city in which the convention is held. A headquarters is maintained in which all information pertaining to gastroenterological subjects is supplied to the profession, and simply for the asking. Meetings are held, usually monthly, in various parts of the country, and a journal is issued once a month to publish important papers. The headquarters is at 33 West 60th Street, New York 23, N. Y.

ANTHONY BASSLER, M.D., F.A.C.G.

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#### OUR SECOND QUARTER-CENTURY

With this issue we begin our twenty-sixth year of continuous publication, all of them as the official journal of the American College of Gastroenterology, the present name of the parent organization. Ours was the pioneer journal of gastroenterology, proctology and allied subjects in the United States and Canada.

From a small quarterly in 1934 to our present size monthly magazine, we have always sought to bring to our readers the best in the field. Our emphasis has been and will continue to be on clinical material, which together with research articles, abstracts of current literature, book reviews and editorials on pertinent matters make up the pages of our journal.

As we take leave of our Silver Anniversary Year, we salute those who have helped us during our first quarter of a century and look forward to their continued valuable assistance in the years to come.



### *President's Message*

An Annual Convention is a necessary and important function of any organization. So, too, in the American College of Gastroenterology does our Annual Meeting fulfill a vital function. It affords an opportunity for the officers, the Board of Trustees and the

Board of Governors to meet and what is more important, enables the membership to come together for an exchange of ideas pertinent to gastroenterology.

This latter aim is best attained through the presentation of papers, both at the Convention and the Postgraduate Course which follows. The number of members who have appeared on our program in the past years has currently increased and I should like to see this trend continue.

The panel discussions have been made up almost entirely of the top men on the faculties and staffs of the local medical schools. The speakers for the Postgraduate Course have, for the most part, all been chosen from the medical schools, by invitation. They have presented their papers with comments by the outstanding medical and surgical co-ordinators, selected by the College especially for the instruction of young gastroenterologists.

Applications to present papers at the 1959 Convention in Los Angeles have already gone out to the membership and on behalf of the program chairman, I request your aid in seeing to it that they are completed and returned no later than 15 January 1959.

I want to take this opportunity to wish the entire membership of the American College of Gastroenterology the Season's Greetings and Good Wishes for a Happy, Healthy and Successful New Year.

*Frank J. Borrelli*

## NEWS NOTES

### NEW COLLEGE OFFICERS FOR 1958-1959

Dr. Frank J. Borrelli of New York, N. Y., assumed the Presidency of the American College of Gastroenterology at the Annual Banquet in New Orleans, La., on Tuesday, 21 October 1958, succeeding Dr. C. Wilmer Wirts of Philadelphia, Pa.

Dr. Wirts was elected Chairman of the Board of Trustees at a Special Meeting of the Board of Trustees which was held in New Orleans on Wednesday, 22 October 1958.

On Sunday, 19 October 1958 at the Annual Meeting of the American College of Gastroenterology, at the Jung Hotel, Dr. Joseph Shaiken of Milwaukee, Wisc., was selected as President-elect. Dr. Shaiken will assume the Presidency at the Annual Meeting in Los Angeles in September of 1959.

Elected Vice-Presidents were Drs. Henry Baker, Boston, Mass.; Louis Ochs, Jr., New Orleans, La.; Edward J. Krol, Chicago, Ill. and Theodore S. Heineken, Glen Ridge, N. J. Dr. Joseph R. Van Dyne of Forest Hills, N. Y., was elected Secretary.

Elected Trustees for three years each were: Drs. Harry Barowsky, New York, N. Y.; Robert R. Bartunek, Cleveland, Ohio; Donald C. Collins, Hollywood, Calif.; Harry A. Oberhelman, Oak Park, Ill. and Henry G. Rudner, Sr., Memphis, Tenn.

Governors elected were: Drs. Fred E. Manulis, Palm Beach, Fla.; Maxwell R. Berry, Atlanta, Ga.; John P. Waitkus, Chicago, Ill.; Joseph E. Walther, Indianapolis, Ind.; Elwood Buchman, Iowa City, Iowa; Sam A. Overstreet, Louisville, Ky.; William Fisher, New Orleans, La.; Edward J. Nightingale, New York, N. Y.; A. Jack Tannenbaum, Greensboro, N. C.; Stanley S. Sidenberg, Cleveland, Ohio; William L. Leet, Providence, R. I.; Ralph R. Braund, Memphis, Tenn.; H. B. Eisenstadt, Port Arthur, Texas; Emile Gribovsky, Huntington, W. Va. and Paul Letendre, Montreal, Quebec.

Dr. Dale W. Creek of Santa Barbara, Calif., was elected Chairman of the Board of Governors at their meeting on Tuesday, 21 October 1958.

Re-elected by the Board of Trustees were Dr. Lynn A. Ferguson, Grand Rapids, Mich., Secretary-General; Dr. William C. Jacobson, New York, N. Y., Treasurer and Dr. Samuel Weiss, New York, N. Y., Editor-in-Chief.

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### WOMEN'S AUXILIARY ELECTS

At their Annual Meeting in New Orleans on Sunday, 19 October 1958, the Women's Auxiliary inaugurated Mrs. S. Bernard Kaplan of Maplewood, N. J.,

as the incoming President. Mrs. Kaplan Was President-elect, selected at the meeting last year in Boston.

Newly elected officers for 1958-1959 are: Mrs. Theodore S. Heineken, Glen Ridge, N. J., President-elect; Mrs. Dale W. Creek, Santa Barbara, Calif., 1st Vice-President; Mrs. George K. Wharton, Los Angeles, Calif., 2nd Vice-President; Mrs. Murrel H. Kaplan, New Orleans, La., Recording Secretary; Mrs. William W. Abrams, Kansas City, Kans., Corresponding Secretary and Mrs. Joseph R. Van Dyne, Long Beach, N. Y., Secretary.

#### FELLOWSHIPS IN GASTROENTEROLOGY

Two additional fellowships for graduate training in Gastroenterology are now available at The Jefferson Medical College and Hospital in Philadelphia, Pa., Stipend up to \$4500 per annum. A minimum of two years of medical residency is a prerequisite. Apply to C. Wilmer Wirts, M.D., Associate Professor of Medicine.

#### INTERNATIONAL CONGRESS OF GASTROENTEROLOGY

The 6th Meeting of the Association of the National European and Mediterranean Societies of Gastroenterology, organized by the Association of Dutch Gastroenterologists, will be held in Leiden, the Netherlands, from 20 to 24 April 1960.

The main themes of the conference will be: 1. Pathology of the small intestine; 2. Hepatitis, Cirrhosis hepatitis and their possible connection.

Panel discussions, lectures and film shows will be arranged in connection with these themes and related subjects. Scientific and technical-commercial exhibits will also be organized.

Original reports on these subjects or any other gastroenterological subject, either clinical or in the field of the basic sciences, are invited for submission and will be accepted for panel discussion or publication if approved by the Scientific Program Committee.

Titles for papers together with a summary of not more than 200 words should be sent not later than 1 August 1959, to Dr. B. K. Boom, Congress Office, Department of Gastroenterology, University Hospital, Leiden, the Netherlands.

Registration fee (including an official reception, a banquet and an excursion) full member: \$45, accompanying family members: \$20.

After 1 November 1959, the registration fee for full members will be \$55.

The fees quoted in U.S. dollars can be paid also in Dutch guilders or any other transferable currency.

For further information and registration apply to the Congress Office of the 6th Meeting of the Association of the National European and Mediterranean Societies of Gastroenterology, Department of Gastroenterology, University Hospital, Leiden, the Netherlands, or the Secretary of the national societies of gastroenterologists.

## In Memoriam

We record with profound sorrow the passing of Dr. M. E. Gabor of Milwaukee, Wisc., Associate Fellow and Dr. Henry B. Steinbach of Gulf Stream, Fla., Fellow of the American College of Gastroenterology. We extend our deepest sympathies to the bereaved families.

**SIGN OF GOOD TASTE**

## ABSTRACTS FOR GASTROENTEROLOGISTS

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### GASTROINTESTINAL TRACT

**PRURITUS AS A SYMPTOM OF INTERNAL DISEASE:** Stephen Rothman. *Am. Pract. & Digest. Treat.* 9:226 (Feb.), 1958.

The internist is primarily interested in those conditions in which generalized pruritus is caused by systemic diseases without the presence of actual skin lesions. These diseases are diabetes, hepatic diseases with and without bile obstruction, lymphoblastomas, internal malignancies and kidney insufficiencies.

In pruritus ani, the author has found a 50 per cent association with atopic dermatitis (neurodermatitis) and has rarely seen proctitis, colitis, intestinal parasites, hemorrhoids or diabetes as an etiologic factor. In the other 50 per cent the complaint is purely psychoneurotic or a functional disease. It starts with some banal irritation and continues with a never ending itching cycle producing lichenification. He recommends

sitz-bath instead of toilet tissue, soothing pastes, minimal doses of soft x-rays and barbiturates.

In jaundice, itching is seen in 20 to 25 per cent of cases and is due to the accumulation of bile salts. There is a higher percentage of pruritus in jaundice caused by neoplasms, common duct obstruction and to drug poisoning.

Pruritus due to internal malignant true neoplasm is rare but does occur. Combined with hyperpigmentation, it is seen in carcinomas of the gastrointestinal tract, carcinoma of the breast, bronchi, pancreas, uterus, sarcoma of the thyroid gland. The pruritus seems to be due to toxic decomposition products of the tumor.

SAUL A. SCHWARTZ

### ESOPHAGUS

**CARCINOMA OF THE ESOPHAGUS:** David P. Boyd, Herbert D. Adams and Ferdinand A. Salzman. *New England J. Med.* 258:271 (6 Feb.), 1958.

The authors review the changing concepts in the management of carcinoma of

the esophagus. Their experience is based on 335 cases of cancer of the esophagus

with particular attention to a smaller recent group that had intensive treatment with a 2,000,000-volt x-ray apparatus in addition to surgical therapy.

Esophageal cancer accounts for slightly less than 2 per cent of all cancer deaths in this country. However, the paucity of reports in the literature indicates the relative lack of interest by surgeons presumably due to the variety and magnitude of the problems encountered and the indifferent results that have been obtained.

The pattern of spread is important to an understanding of the problems encountered in treatment. Esophageal cancer spreads along the mucosa and submucosa and may set up satellite lesions at a distance from

the primary lesion. In 68 per cent of the cases there is direct extension with involvement of neighboring lymph nodes. While widespread dissemination is frequently found it is usually a late event.

Results are poor because of the extreme malignancy of esophageal cancers, an anatomical relationship that involves vital structures and a construction that makes surgical manipulation extremely difficult. Although their series is small the authors feel that partial or complete surgical extirpation followed by supervoltage x-ray therapy may be the preferred mode of treatment than by any other means.

LOUIS A. ROSENBLUM

#### ACUTE MASSIVE GASTROINTESTINAL HEMORRHAGE: Roy Cohn. *Med. Times* 86:129 (Feb.), 1958.

Since approximately 70 per cent of patients with liver cirrhosis who present massive gastrointestinal hemorrhage will die directly of the hemorrhage or the complications which follow, active attempts have been made to control the hemorrhage at its source.

The author has found the balloon tubes, which exert direct pressure on the esophagus, too difficult to use, especially in alcoholics, and he advocates a surgical approach to the problem.

As these patients are usually in a poor

general condition, anastomosis or resection is considered too extensive, and the attempt is therefore made to ligate the involved varix directly whenever possible.

It is the author's belief that such an operative procedure with ligation of a bleeding varix in the cirrhotic can salvage a few, who would otherwise die of hemorrhage.

The author also emphasizes that hemorrhage can occur from other areas than just the esophagus.

H. J. JOSEPH

#### STOMACH

#### A BRIEF REVIEW OF DIAPHRAGMATIC HERNIA: Robert G. Wochos. *Wisconsin M. J.* 56:273 (June), 1957.

This brief but informative article discusses the types of diaphragmatic hernias, their origin, and their treatment.

More than 75 per cent of the diaphragmatic hernias are of the esophageal hiatus type and the majority of these are of the direct variety. The author gives the common symptoms of each type and then dis-

cusses treatment. Operative technic as given is somewhat sketchy but he takes into consideration the type of approach, whether transthoracic or abdominal, that would be applicable in each of five illustrative cases presented. A bibliography is appended.

PAUL B. VAN DYKE

#### MANAGEMENT OF THE DUODENAL STUMP: Nicholas J. Capos. *Quart. Bull. Northwestern Univ. M. School* 31:297 (Winter), 1957.

It has been long recognized that one of the most dangerous complications for the gastric surgeon is the "blown-out" duodenal stump. This complication occurs between the third and tenth postoperative days.

The author reviews the problem from the different methods of handling the dangerous situation such as Dragstedt's procedures of vagotomy and posterior gastroenterostomy. Bancroft-Plenk in their closure

of the duodenal stump transect the stomach 6 cm. proximal to the duodenal stump. Mucus is removed to the pyloric sphincter and then the pylorus closed by interrupted silk sutures and the 2-layer imbrication of the antral muscularis with interrupted 4-0 silk.

If no method is applicable a No. 18 French rubber catheter may be inserted and pursestrung. This is brought out of the abdomen then in separate stab wound. Mild suction is applied. After 8 to 12 days the catheter is removed.

If the duodenal stump "blows out" an

emergency operation must be performed and a Chaffin tube is inserted down to the area of the rupture and suction applied. If drainage is too profuse a Witzel type jejunostomy must be performed to keep the electrolytes balanced properly.

In summary, it must be emphasized that the type of closure of the duodenum where complications of the ulcer are present must be based on the estimate of the surgical problem and then try to do that method that best fits the difficulty at hand.

I. HENRY EINSEL

**INCIDENCE OF MEGLOBLASTIC ANEMIA AFTER SUBTOTAL GASTRECTOMY:**  
Lloyd D. MacLean. *New England J. Med.* 257:262 (8 Aug.), 1957.

Megaloblastic anemia indistinguishable from pernicious anemia is a late but inevitable sequel of total gastrectomy and probably of proximal subtotal gastrectomy with esophagoantrostomy.

It is suggested that patients who are capable of producing adequate quantities of intrinsic factor when endowed with an intact stomach may be rendered deficient

in this capacity if the stomach is subtotally resected.

It is believed that patients likely to have megaloblastic anemia after subtotal gastrectomy can be predicted by microscopical examination of the resected portion of the stomach.

JACOB A. RIESE

**SOME NOTES ON THE PATHOGENESIS OF DUODENAL ULCER:** J. N. Hunt. *Am. J. Digest. Dis.* 2:445-453 (Sept.), 1957.

If peptic ulcer may be regarded to result from a disturbed equilibrium between the digestive power of the secretion and the tissue's ability to resist it, then in most patients with gastric ulcer the mucosal resistance appears to be subnormal, while in most patients with duodenal ulcer the digestive power of the secretion seems to be supranormal. The majority of the data on the hypersecretion of acid in patients with

duodenal ulcer can be satisfactorily accounted for by supposing that they have more than the usual number of acid-secreting and pepsin-secreting cells. In some patients there is also a failure of the mechanism which inhibits gastric secretion. It has not been possible to show that gastric emptying is unduly rapid in patients with duodenal ulcer.

WALTER CANE

**GLUTAMINE IN TREATMENT OF PEPTIC ULCER:** William Shive, R. N. Snider, Ben DuBilier, Joe C. Rude, George E. Clark, Jr. and Jerome O. Ravel. *Texas J. Med.* 53:840 (Nov.), 1957.

This preliminary study of a group of 57 patients with peptic ulcer analyzes the results when 46 of these received glutamine. Of these 46, 12 patients also were treated with antacid and antispasmodics. Since the results from the preliminary study giving combined and conventional and glutamine therapy was encouraging, a series of 24 patients were treated with glutamine alone. These patients were instructed not to change their diet except to omit alcohol or

highly seasoned or fried foods. No medication other than glutamine was administered unless it had been administered for more than six months before the discovery of the present ulcer. Of these 24 patients, the ulcers of 12 healed by the first radiological reexamination in two weeks and the ulcers of eight more patients healed by the second reexamination in approximately four weeks. A double-blind study was then performed with 21 patients given either lactose or

glutamine in addition to a regimen of diet, antispasmodics and antacid therapy. In this double-blind test there was apparently a statistically significant increase in the rate

of healing in those patients who had received glutamine. This series, however, is far too small to draw any conclusions.

RALPH D. EICHORN

**HODGKIN'S DISEASE OF THE STOMACH:** Max Thorek, Benjamin Ebert and Rodolfo Duran. *J. Internat. Coll. Surgeons* 28:532 (Nov.), 1957.

Hodgkin's disease, an infectious granulomatous affliction of unknown etiology, is a rare occurrence in the stomach. In a review of 16,254 autopsies, Mead discovered only 3 cases of isolated Hodgkin's involvement of the gastrointestinal tract. In three different series of proven Hodgkin's disease gastric involvement was found in 1 out of

212 cases; 2 out of 54 cases and 1 among 319 cases respectively.

Clinically, it is almost impossible to distinguish Hodgkin's disease of the stomach from carcinoma of the stomach in the absence of overt Hodgkin's disease in other areas.

EZRA J. EPSTEIN

**IMPORTANCE OF THE GASTRIC BRUSH IN THE DIAGNOSIS OF CANCER:** Juan Nasio. *Med. Times* 85:1383 (Dec.), 1957.

The survival rate of cancer of the stomach is in direct proportion to early surgical intervention which is, naturally, directly related to early diagnosis.

The Ayre brush technic for obtaining cellular material from the stomach has been found by the author to be best suited to office practice. It is superior to other methods for collecting gastric cells. The advantages of this method are:

1. The bristles of the brush directly contact the gastric cellular material.
2. Because of its length the brush reaches the pyloric antrum.
3. The cells are neither mutilated or lost.
4. Washing out the stomach is obviated.

5. The cells do not need to be washed or centrifuged and therefore can be transferred to a glass slide and fixed immediately.

In 85 patients clinically suspected of having gastric malignancy, excluding those with obvious clinical or radiological evidence of such a malignancy, the diagnostic results of the gastric brush technic revealed: Positive—60 per cent; Suspicious—30 per cent; False Negative—10 per cent.

The Ayre technic, as indicated, becomes an important diagnostic tool in establishing a definite diagnosis of gastric cancer, especially if a surgical biopsy via gastroscopy is unobtainable.

EZRA J. EPSTEIN

**PRIMARY MULTIPLE GASTRIC CARCINOMA WITH UNUSUAL HISTOLOGIC CHARACTER:** Kazim Ismail Gurkan. *J. Internat. Coll. Surgeons* 28:739 (Dec.), 1957.

This is a case report of one case of multiple gastric carcinoma, wherein microscopic section through the first growth, showed highly differentiated epidermoid carcinoma

and section through the second tumor showed well differentiated adenocarcinoma.

RALPH D. EICHORN

**HYPOGLYCEMIA FOLLOWING PARTIAL GASTRECTOMY:** C. M. B. Pare. *Am. J. Digest. Dis.* 3:1-11 (Jan.), 1958.

Compared with the literature on the commoner and more dramatic dumping syndrome, very little has been written on the late postprandial hypoglycemic symptoms after partial gastrectomy although the latter may be severe enough to cause unconsciousness. Between the two schools of

thought as to its cause, i.e. anatomic-physiologic vs. hormonal changes secondary to gastric resection, the author comes out in favor of the latter. In a cogent manner, both as to his experiments and as to his way of reasoning, he concludes that adrenal cortical insufficiency in the stress phase of

Selye's general adaptation syndrome after the operation deserves serious consideration particularly as cortisone relieved the symptoms in such individuals without affecting

their blood sugar levels or their glucose tolerance curves.

WALTER CANE

**MEDICAL MANAGEMENT OF PERFORATED PEPTIC ULCER: M. Murray Schechter.**  
**J. M. A. Georgia 47:10 (Jan.), 1958.**

While not contesting that the treatment of perforated peptic ulcer is primarily surgical, the author lists six situations when medical management might be preferred: *Formes frustes*, poor risk patients, late perforations, equivocal diagnosis, unavailable competent surgery and when perforations of less than twelve hours show improvement.

The salient features of medical management include the following: 1. Gastric suc-

tion by the Levin tube. 2. Antibiotic therapy with penicillin and streptomycin. 3. Neutralization of acid by intragastric drip or frequent Sippy feedings. 4. Supportive therapy with infusions including potassium and whole blood if necessary.

In rare instances parenteral cortisone served to counteract severe or intractable shock due to the perforation state.

A. M. SUSINNO

**A NEW ANTICHOLINERGIC AGENT IN THE TREATMENT OF PEPTIC ULCER:**  
**Nicholas C. Hightower, Jr. and A. Compton Broders, Jr. Texas J. Med. 54:83 (Feb.), 1958.**

A new prolonged action anticholinergic drug, a brand of propantheline bromide (Pro-Banthine) was used by the authors on 15 cases with active symptoms of peptic ulcer. One 30 mg. tablet was given before breakfast, and another tablet, 30 mg., at bedtime. A Sippy diet regime plus antacids were used. The results of therapy were considered excellent for 10 of their 15

patients, with the patients becoming asymptomatic within 24 to 72 hours. Only two of the patients experienced undesirable side-effects. The fact that the patient is required to take only two tablets (30 mg. each) daily for satisfactory results, affords patient-acceptance of the medication.

SAMUEL M. GILBERT

**CLINICAL EXPERIENCE WITH 31 CONSECUTIVE CASES OF SURGICAL INTERVENTION FOR THE CONTROL OF BLEEDING FROM THE UPPER GASTRO-INTESTINAL TRACT: James M. Parker. New England J. Med. 258:417 (27 Feb.), 1958.**

The author describes his experience with 31 consecutive cases of bleeding from the upper gastrointestinal tract. This experience appears to parallel that of other observers who have written on this subject. Diagnosis

is based on history and emergency x-ray study. Surgery is performed for persistent bleeding for more than 48 hours.

ABE ALPER

**TOTAL GASTRECTOMY FOR CARCINOMA: I. Boerema. J. Internat. Coll. Surgeons 29:135 (Feb.), 1958.**

The end results of gastric resection for carcinoma are still disappointing and one must do a block excision for gastric carcinoma. This procedure must include some removal of the esophagus, the duodenum, the whole lesser omentum, the gastrocolic ligament, the spleen, the tail of the pancreas, and the retroperitoneal lymphatic tissue of the upper part of the abdomen.

By means of this technic the supradiaaphragmatic anastomosis between the esophagus and the jejunum can be made trans-abdominally with an improved Murphy button. Fatality rate is diminished using this procedure and patients up to 70 years of age stand the procedure fairly well.

The author defends total gastrectomy in all cases of gastric carcinoma except the

prepyloric. The author reports a total number of 117 cases; 83 per cent went back to work leading a normal life. The most important factor which might cause trouble is the question of a sufficient quantity of food. Many of these gastrectomized patients have

lost their appetites and it is necessary to prescribe the quality and quantity of food eaten in order to avoid undernourishment. Nitrogen and fat loss by stool were compensated for by higher intake.

ABRAHAM BERNSTEIN

**DUODENAL ULCER AS AN ETIOLOGIC FACTOR IN GASTRIC ULCERATION:**  
**Jack D. Ballard and J. Thomas Payne. Northwest Med. 57:193 (Feb.), 1958.**

This is a study of 59 patients with gastric ulcer of whom one-third had duodenal ulcer in association with gastric ulcer. The authors believe that duodenal ulceration or malfunction usually appears first when found with gastric ulcer and may be related to the pathogenesis of the gastric ulcer. Others have also noted that in co-existing gastric and duodenal ulceration relief of duodenal obstruction is often fol-

lowed by disappearance of the gastric ulcer. The authors conclude that gastric ulcer associated with duodenal ulcer is best treated by gastric resection, and that medical treatment of such combined lesions may be difficult or impossible. In gastric ulcer without concomitant duodenal ulcer malignancy must be considered.

ARNOLD STANTON

**THE VOMITING CHILD: F. H. Bentley. Northwest Med. 57:189 (Feb.), 1958.**

The author emphasizes certain points in the diagnosis of a vomiting child. The important points to note are the mode of onset (salivation of the newborn, regurgitation after some days of normal feeding, or the sudden crying of a healthy child), the progression of symptoms (the surgical abdomen tends to get worse), and the presence of certain physical signs, such as the

character of the vomitus, abdominal distention, abdominal tenderness, and the presence of a lump. Laboratory findings are not in themselves of particular diagnostic value. The diagnosis of a surgical lesion in a vomiting child is largely a matter of clinical judgment and skill.

ARNOLD STANTON

**GASTROILEOSTOMY WITH REALIGNMENT AND RECOVERY: Alfred Haas and Saul Alfred Ritter. J. Internat. Coll. Surgeons 29:155 (Feb.), 1958.**

Gastroileostomy is usually a surgical error occurring during the course of a gastro-enterostomy or partial gastrectomy.

The clinical picture is that of diarrhea containing undigested food, malnutrition, dehydration, hypoproteinemia, and marked weight loss coming on just after surgery. Gastroileal ulcers with hemorrhage and pain have been reported. Most of the symptoms are due to the passage of food into the ileum before it has been acted upon by the digestive enzymes.

The clinical syndrome must be differentiated from a gastrojejunocolic fistula which also may result after peptic ulcer surgery.

Here the onset usually follows a period of good health and is accompanied by milder symptoms. Radiographic studies confirm the diagnosis in either case.

Prevention of a gastroileostomy entails proper identification of the ligament of Treitz and the marking of the proximal jejunum with stay sutures.

Treatment in the case reported consisted of freeing the old anastomosis, resecting the involved ileum, and the establishment of a retrocolic Hofmeister gastrojejunostomy.

THEODORE COHEN

**GASTRIC DIVERTICULUM: Duncan Shepard. J. M. A. Georgia 47:65 (Feb.), 1958.**

Gastric diverticula occur at any age predominantly in the juxtaesophageal area on

the posterior wall of the stomach. They are usually due to a congenitally weak spot

where the longitudinal muscle fibers spread out. They are almost always single, and are true diverticula.

Most juxtaesophageal diverticula are asymptomatic, although at times they may be accompanied by epigastric pain radiating to the retrosternal area, vomiting, dysphagia, distention and bleeding. Lying down may aggravate the pain. When a diverticulum is found, however, one must be certain that there is no other gastrointestinal pathology present before incriminating it.

Radiographic studies reveal the lesion best in the lateral or oblique views with

the patient in the Trendelenburg position. Rugal folds may be seen running into the opening.

The most common complications are bleeding which is rarely massive, torsion with gangrene, rupture and perforation.

Treatment in symptomatic cases consists of frequent feedings, bland diet, and alkali. Indications for surgery are persistent symptoms, massive or recurrent bleeding, or the question of the presence of a malignancy. Simple excision gives uniformly good results.

THEODORE COHEN

## INTESTINES

### THE MANAGEMENT OF PERFORATIVE CARCINOMA OF THE COLON: Gordon A. Donaldson. *New England J. Med.* **258**:201 (30 Jan.), 1958.

Albrecht von Haller (1708-1777), described, in 1775, the first cologastric fistula due to cancer, but until 1953 only 156 cases were recorded in the literature, with a survival of 6.

A study of technics over the past 20 years of 186 cases, comprising 7.8 per cent of all colonic carcinoma cases admitted to Massachusetts General Hospital, shows that primary attack has a direct bearing on mortality.

All cases were placed in three categories:

1. Free rupture into abdominal cavity.
2. Those leaking locally, forming abscesses.
3. Those rupturing into a nearby viscus.

Because of inflammatory processes 50 per cent of all cases fell into category 2.

Widespread contamination occurred when the rupture was in the ascending or descending colon; no contamination when pathology was in the transverse colon; 50

per cent of ruptures in the lower descending colon walled-off in the pelvis.

The older conservative methods of drainage and/or exteriorization have been abandoned for the more direct primary resection in categories 1 and 3, and salvage rates have justified this change in technic.

Primary resection in 41 cases resulted in 2 deaths or 5 per cent mortality.

One hundred and eight patients were treated by preliminary by-passing, and this resulted in 29 per cent mortality; by-pass with peritoneal lavage gave a mortality of 10 per cent, simple drainage 50 per cent.

In this series 68 per cent of 121 patients were subjected to resection, with or without preliminary by-passing, and 84 have survived 5 years postoperatively, and thus it is felt that the more heroic measures have contributed to the larger salvage rate than the heretofore conservative management.

J. EDWARD BROWN

### EXPOSURE IN ABDOMINAL SURGERY: Rex L. Ross. *Northwest Med.* **57**:36 (Jan.), 1958.

The author describes a method of obtaining better exposure in abdominal operations by placing the small bowel covered by a wet laboratory pad into a vinyl plastic bag and then placing the bag with the contained small bowel out on the abdominal wall. In some cases it may be necessary to mobilize the cecum to get all of the small

bowel into the bag.

Vinyl plastic material can be bought at the dime store. It is durable and can be autoclaved. A bag 18" x 16" in size will suffice. The edges may be reinforced with tape. The mouth of the bag can be narrowed by loose ties on the edges.

ALEXANDER ZABIN

**FURTHER OBSERVATIONS ON THE GLUTEN-FREE DIET:** Ivan C. Keever, W. Crockett Chears, Jr. and Julian M. Ruffin. *Am. Pract. & Digest Treat.* 9:74 (Jan.), 1958.

The authors have noted that the elimination of rye and wheat from the diet of children having celiac disease was followed by clinical remissions and its addition resulted in relapse.

Further observations demonstrated that the responsible factor was chiefly in the gluten fraction. Gliadin is the principal prolamin of wheat and the factor in gliadin responsible for celiac disease is still to be identified.

It has been found that administration of gluten-free diet in celiac disease patients resulted in increased rate of growth, weight

gain and diminished fecal fat. Nontropical sprue has also responded to gluten-free diet.

The authors report two cases, one nontropical sprue and the other Whipple's disease, both of which responded favorably to a gluten-free diet.

The exact reason why a gluten-free diet is of value is unknown. A number of mechanisms have been suggested, including hypersensitivity to gluten. Its mode of action still remains a mystery.

LOUIS K. MORGANSTEIN

**THE HAZARDS OF RICHTER'S HERNIA:** Edwin F. Hirsch. *Illinois M. J.* 113:23 (Jan.), 1958.

The author emphasizes the danger of a Richter's hernia, in which only a part of the caliber of the bowel has passed into a pouch. Richter's hernia is usually found in the groin, but can be behind the umbilicus or elsewhere. A brief pathological report is given, emphasizing the hazards of an unreleased Richter's hernia of the small bowel. This type of hernia can occur simultaneously with other types in the same patient and

may be easily confused as to which one is responsible for the symptomatology.

A case report of a white male, 59 years of age is given. The diagnosis on arrival at the hospital was incarcerated left inguinal hernia. The patient died seven hours after admission. The necropsy demonstrated that the site of the obstruction was in the unsuspected Richter's hernia of the umbilicus.

CARL J. DEPRIZIO

**PREOPERATIVE DIAGNOSIS OF MECKEL'S DIVERTICULUM:** Arthur F. Hunter, Willard L. Mathiesen, James L. McMillan and Warren C. Hunter. *Northwest Med.* 57:205 (Feb.), 1958.

The authors report the preoperative diagnosis of a case of Meckel's diverticulum in a 38-year old woman who had repeated bleeding episodes characterized by tarry stools. The signs of Meckel's diverticulum are rectal bleeding, obstruction, intussusception, inflammation, malignant degeneration and the presence of a foreign body. The authors believe that there should be a

high clinical index of suspicion in the minds of physicians, and they advocate a gastrointestinal registry to reveal clinical and radiologic accuracy in diagnosis, and surgical competence in the treatment of Meckel's diverticulum. This would increase our knowledge of the clinical aspects of Meckel's diverticulum.

ARNOLD STANTON

**TRANSPLANTATION OF THE URETERS INTO AN ISOLATED ILEAL LOOP:** J. Harold Newman. *J. Florida M. A.* (Feb.), 1958.

A series of five cases is reported in which urinary diversion was accomplished by ureteroileal anastomosis and ileostomy. This appears to be the safest and most satisfactory type of urinary diversion available at the present time. With the possible ex-

ception of pyelonephritis, the complications which occur are not inherent in the operation and can be eliminated. External drainage is a disadvantage but not a contraindication. The patients do not feel that they are severely handicapped and quickly ad-

just to the new method of micturition. They have been able to resume most of their normal activities and lead relatively

normal lives. There have been no odor or esthetic problems.

BERNARD STERN

## LIVER AND BILIARY TRACT

### THE MANAGEMENT OF INFECTIOUS HEPATITIS: Richard D. Eckhardt. Illinois M. J. 113:10 (Jan.), 1958.

The author studied a total of 260 patients. These were service men and the average age was 21 years. The inflammatory phase of the illness was considered to be over when the total bilirubin was 1.5 mg. per cent or less and the 45-minute BSP retention was below 5 per cent.

The average recovery time for the bed rest group was 27 days, and for the more active group (complete bed rest not enforced) was 24 days. This difference was not considered to be significant. In the group forced to eat a high caloric diet with high protein and vitamin content, recovery was six days earlier than in the group who ate as desired. In about 5 per cent of the men too sick to eat adequately during the first several days after admission, the average recovery was 51 days; whereas, those who were tube-fed in the same very sick group, recovered after only 33 days. The general average for all pa-

tients was about 25 days. The type of diet given, the addition of vitamins, antibiotics, steroids, etc., reveal no significant difference in the time of recovery or comfort of the patient.

It was generally observed that in all groups, the higher the bilirubin level on admission, the longer the illness. The average bilirubin level on admission was 8 to 9 mg. per cent, and the average interval between the onset of symptoms and hospitalization was about 10 days. This is about the same as that noted in civilian outbreaks.

In general, it is agreed that hepatitis in older age groups is far more severe than in the service age groups. The amount of alcohol intake before admission seemed to play no significant part, but it was deemed advisable to caution against any alcohol ingestion for three to six months after the acute illness.

CARL J. DEPRIZIO

### HEPATIC AND RENAL FAILURE: Am. J. Med. 24:122 (Jan.), 1958.

Hepatorenal syndrome is not a specific entity but designates the various renal disturbances associated with severe hepatic disease. Albuminuria, pyuria, hematuria, azotemia, electrolyte deviations, isosthenuria, oliguria and anuria as well as uremia occur in the course of various hepatic disorders. Azotemia, edema, hyponatremia and hypopotassemia may result from prerenal dys-

function, or from the treatment of ascites. Oliguria, anuria, isosthenuria, pyuria and red cells and casts may be due to an associated renal disease; for instance, toxic or deficiency nephropathy, lower nephron nephrosis, pyelonephritis, acute or chronic glomerulonephritis, thrombus and embolism of the renal vessels.

H. B. EISENSTADT

### INDICATIONS FOR COMMON DUCT EXPLORATION: Marshall K. Bartlett and William R. Waddell. New England J. Med. 258:164 (23 Jan.), 1958.

It is the experience of the authors that choledochostomy, if added to cholecystectomy, will triple the postoperative mortality. In 1,280 cases of only cholecystectomy eight deaths or 0.6 per cent were encountered, while in 963 cases of combined operations 17 deaths or 1.8 per cent occurred.

Therefore, in a subsequent tabulation, the authors analyzed 1,000 cases of com-

bined operations in order to be able to formulate exact indications for common duct exploration. These indications—in the order given below—also point to the probable presence of a common duct stone. They are: jaundice, a palpable stone in the common duct, dilated common duct, dilated cystic duct, small stones in the gallbladder, and previous attacks of pancreatitis. De-

tailed tables are presented to back up these postulates.

Previous attacks of pancreatitis constitute an absolute indication for exploring the common duct, in spite of the fact that only a few common duct stones may be found.

It may be of further interest to note that the authors consider any common duct with an outside diameter of one cm. or more,

any cystic duct with an outside diameter of four mm. or more as dilated.

The size of so-called small stones of the gallbladder was given as less than 0.5 cm. in diameter. It is in this latter group, which in the average yields only 16 per cent of common duct stones, that reduction in choledochostomy is indicated.

H. J. JOSEPH

**FURTHER CLINICAL AND INVESTIGATIVE USES OF LIVER BIOPSY: K. L. Stuart, G. Bras, S. J. Patrick and J. C. Waterlow. A.M.A. Arch. Int. Med. 101:67 (Jan.), 1958.**

Liver biopsy with histological as well as chemical examination of the specimens was used to clarify certain diseases, indigenous to Jamaica. 1. Veno-occlusive disease of the liver affects undernourished children and adults. In the acute stage the abrupt onset of hepatomegaly and intractable ascites without previous history of liver disease resembles the Budd-Chiari syndrome. It is caused, apparently, by a sudden blockage of the small centrilobular veins, which show subendothelial swelling of the intima. There is a secondary centrilobular congestion and parenchymal necrosis producing a nutmeg liver. If recovery does not occur a subacute stage with centrilobular fibrosis and finally a chronic stage with nonportal cirrhosis, congestive splenomegaly, recurrent hematemesis and occasionally jaundice will follow. 2. Kwashiorkor and marasmus are related nutritional disturbances mostly in children due to protein deficiencies. Kwashiorkor is characterized by blubbery fat

and edema, marasmus by muscular wasting, dehydration and fat loss. Depigmented hair, cheilosis, stomatitis, glossitis, anemia and hepatomegaly are found in both groups. Marasmic kwashiorkor shows a mixture of symptomatology. Fatty liver with mild degenerative changes of parenchymal cells is a characteristic finding in all these nutritional disorders. Also an excessive amount of glycogen is present in the cells in addition to the fat accumulation. 3. Vomiting sickness of Jamaica is characterized by extreme hypoglycemia and marked loss of liver glycogen. It may be caused by eating an unripe fruit (ackee) which has a marked hypoglycemic activity. Vomiting, diarrhea, fever, convulsion, coma and death are observed in this disorder. 4. Various nutritional neuropathies are seen in Jamaica in association with hepatic fibrosis. Also a high incidence of hepatic fibrosis is associated with sickle cell anemia in this locality.

H. B. EISENSTADT

**CHRONIC IDIOPATHIC JAUNDICE: I. N. Dubin. Am. J. Med. 24:268 (Feb.), 1958.**

Chronic idiopathic jaundice is a new name suggested for the benign, chronic, or recurrent intermittent jaundice with lipofuscin pigment deposit in the liver, generally known as Dubin-Johnson disease. It begins mostly in childhood or in early adulthood but may be discovered for the first time at any age. It does not favor any sex; it has been observed only once in a negro among the 50 cases so far reported in the literature. There is frequently a typical family history of jaundice. Symptoms of abdominal pain in the region of the liver, weakness, fatigue, anorexia, nausea, vomiting and diarrhea occur during the attacks. Also heartburn, belching, headaches and nervousness are occasionally encountered.

The liver is frequently enlarged, the urine is dark and the stools may be pale. Both direct and total bilirubin in serum are increased, the direct bilirubin amounts to more than 60 per cent of the total. BSP retention, cephalin and thymol turbidity are abnormal only during the attack of jaundice, otherwise all liver function tests are normal. Serum alkaline phosphatase is normal or only slightly elevated. Oral and intravenous cholecystography do not visualize the gallbladder at all or show it only faintly.

Cholelithiasis without bile passage obstruction has been associated in some cases. The liver biopsy is macroscopically characterized by a green-black or a grey bluish

color, microscopically by a deposit of coarse brown pigment granules in the centrolobular hepatic cells. No pigmentation occurs in other organs. The attack of jaundice may come on suddenly or gradually, or it may follow in the wake of pregnancy, various infections especially upper respiratory infections, immunizations, operations, physical and mental stress, during mental illness, or intake of larger quantities of alcohol. Prognosis is excellent as no change of liver cell pattern occurs with time. The cause is supposed to be an inherited metabolic weak-

ness of excretion of bilirubin glucuronic acid. This water soluble substance is regurgitated into the blood and partly excreted into the urine. Inability to excrete BSP and x-ray media must be closely related to the bilirubin dysfunction. Differentiation from obstructive jaundice is based on lifelong history of jaundice, youth of patient, and normal alkaline phosphatase; distinction from Gilbert's disease by dark urine, direct bilirubinemia, failure of BSP and x-ray dye excretion.

H. B. EISENSTADT

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**COMMON BILE DUCT STONES:** Bentley P. Colcock and Harold V. Liddle. *New England J. Med.* **258**:264 (6 Feb.), 1958.

In a three-year period 1,077 patients who had operations on the biliary tract were selected for study. Of this group 948 had cholelithiasis and of these 389 (36.1 per cent of the total) had explorations of the common duct. One hundred thirty-eight (35.5 per cent) had common duct stones. The study was arbitrarily based upon the first 100 consecutive patients whose initial common duct exploration was done at the clinic during this period. Ninety-four had a follow-up period of four to six years, in the remaining it was one year.

The problem of retained stones is primarily related to the patient who has or has had stones in the common bile duct. The authors believe that any long-standing ob-

struction of the common duct predisposes to the formation of stones. Sphincterotomy should also be seriously considered in any patient who has recurrent common duct stones after a choledochostomy for calculi. While hospital stay may be increased a few days by common duct obstruction it was the authors' experience that mortality was not increased. They conclude that "gentle, thorough exploration of the biliary ducts remains a satisfactory means of ruling out stones in the common or hepatic duct." Cholangiography is not a substitute for an adequate clinical evaluation at the operating table.

LOUIS A. ROSENBLUM

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## PANCREAS

**THE LABORATORY DIAGNOSIS OF PANCREATIC DISEASE:** Richard L. Sterkel and Joseph B. Kirsner. *A.M.A. Arch. Int. Med.* **101**:114 (Jan.), 1958.

Serum amylase is still the most widely used test for the diagnosis of acute pancreatitis. It will be elevated also in a considerable number of cases of chronic pancreatitis and carcinoma. Early in the course of acute pancreatitis the largest numbers of positive results are obtained. False positive findings occur in diseases of the biliary tract, spasm of the sphincter of Oddi, mumps, renal insufficiency, penetrating and perforating ulcers, and intestinal obstruction.

Serum lipase should be used more often. It still has some technical shortcomings. False positive tests may be obtained under conditions that give a false elevated serum amylase.

Elevation of plasma antithrombin activity occurs with increased release of trypsin into the blood stream. The specificity of this test for pancreatic disease remains to be evaluated.

Provocative pancreatic enzyme tests after administration of opiates, secretin and cholinergics have proved disappointing.

Diabetic glucose tolerance curve may be helpful and should be used more often in suspected pancreatic disorders.

Serum calcium, serum carotene, fecal fat and fecal nitrogen, absorption of radio-iodinated fats or proteins, starch and Vitamin A tolerance tests and radiophospholipid synthesis are nonspecific investigations.

Urinary amylase and lipase require 24-

hour sampling. They may be helpful within limits in the diagnosis of pancreatic disease.

D-xylose tolerance is normal in pancreatic and impaired in nonpancreatic mal-absorption syndromes.

Secretin test with duodenal intubation is useless in acute pancreatitis. In chronic

blockage of pancreatic ducts usually caused by malignant growth there is a decreased volume response while in chronic inflammatory disease there is a decreased bicarbonate concentration.

H. B. EISENSTADT

**TRUAMATIC PANCREATIC CYSTS:** Lorin D. Whittaker. *Illinois M. J.* 113:1 (Jan.), 1958.

Pancreatic cysts are rare and are found in about one to each 25,000 to 50,000 admissions. Many classifications of pancreatic cysts have been made. The author places them under three headings: the pseudocyst; the true retention cyst; and the group of cystadenomas.

The pseudocyst is the most frequently reported type, comprising about 50 per cent of cases. Physical trauma is frequently mentioned as the etiological factor. The second group, consisting of the true retention cyst, comprises about 25 per cent of the cases reported. True retention cysts are thought by many to result from pancreatic duct obstruction, or by proliferation of acinous tissue with cyst formation. The majority are unilocular. The third group are the cystadenomas and they comprise about 20 per cent of the total admissions. They are usually multilocular and are lined with epithelium, and about one-third are malignant.

The symptoms and clinical signs of pancreatic cysts are given. However, roentgen examination is of the utmost value and the most valuable sign.

Treatment for all pancreatic cysts is surgical. There are three basic operations, namely: excision of the cyst, external drainage by marsupialization, and internal drainage by anastomosis to some part of the upper gastrointestinal tract. The cyst may be approached through the gastrohepatic or gastrocolic omentum.

Complete excision carries a mortality rate of about 10 per cent. The mortality in external drainage by marsupialization is about 4 per cent.

The author reports two cases of traumatic pseudocysts of the pancreas as the result of injury. Both cases were operated upon and made an uneventful recovery. The surgical procedures are given in detail.

CARL J. DEPRIZIO

**PANCREATITIS ACUTE AND RECURRENT MEDICAL MANAGEMENT:** Alexander Rush. *Am. Pract. and Digest. Treatment* 9:50 (Jan.), 1958.

The author divides pancreatitis into three types:

1. *Acute interstitial pancreatitis* comprises 75 per cent, pathology is limited to edema and clinical symptoms range from mild to moderately severe. Improvement is rapid and mortality rate is low—3-4 per cent.

2. *Acute hemorrhage pancreatitis* 15 per cent and pathology is characterized by necrosis and hemorrhage. Clinical symptoms are severe and accompanied by shock and paralytic ileus. Response is variable and improvement delayed. Mortality rate is 45 per cent.

3. *Acute suppurative pancreatitis* 10 per cent and pathology is that of acute inflammation with bacterial infection and formation of large collections of pus. Clinical symptoms are severe and have signs of

abdominal inflammatory mass. Medical response is poor and must resort to surgery. Mortality is 50 per cent.

*Indications for medical management* are the treatment of choice for primary acute pancreatitis, if diagnosis is sure, no mechanical obstruction of biliary tree, no suppuration and no cystic accumulation in abdomen.

*Principles of medical management:*—1. Relief of pain—analgesics, Demerol, morphine, antispasmodics, etc. Use of amyl-nitrate inhalation, aminophyllin, nitroglycerine, papavarine, etc. As autonomic blocking agents use of atropine sulfate, Banthine, Pro-Banthine, tetraethyl ammonium chloride, hexamethonium bromide. For anesthesia use of procain hyd. i.v. 10-20 c.c. 0.1 per cent. Paravertebral block with 1

per cent procain hyd. Splanchnic block with 20-30 c.c. 1 per cent procain hyd.

2. Treatment of shock—must maintain normal blood volume and electrolyte balance. Use of whole blood or normal serum-albumin if needed. Levophed to prevent peripheral vascular collapse. Addition of cortisone or hydrocortisone in the i.v. may be life saving. Glucose and saline to replenish loss of water and electrolytes. Ca Gluconate if calcium loss is suspected.

3. Suppression of pancreatic secretion—nothing by mouth. Maintain continuous suction of stomach, and use of antisecretory drugs as atropin and the anticholinergics.

4. Maintenance of nutrition and carbohydrate metabolism—use of invert sugar (5 per cent dextrose and 5 per cent fructose). Insulin, should hyperglycemia develop. Parenteral multivitamins.

5. Prevention of infection and suppuration—use of antibiotics such as Dicrysticin fortés twice daily is recommended.

6. Maintenance of close observation for

signs of progression of disease and surgical interference. Signs to look for are fall in blood pressure, rise in pulse rate, diminished output of urine, abdominal tenderness, tympany of upper abdomen, with reduced or absent peristaltic sounds, dullness in flanks indicating fluid, sudden rise in temperature with leucocytosis, and finally presence of abdominal mass are indications for surgery.

7. Medical measures during recovery phase—begin oral diet slowly with hourly liquid feedings low in fat and small in volume. Use of antacids, atropin, and anticholinergics.

8. Medical measures during remission—75 per cent develop chronic relapsing pancreatitis. Use 3-4 bland meals a day, small, low in roughage and secretory stimulants. Continue use of antacids and antisecretory drugs. Combat iron deficiency anemias, use of vitamin supplements, etc.

LOUIS K. MORGANSTEIN

## PATHOLOGY AND LABORATORY RESEARCH

**BILIRUBIN METABOLISM IN JAUNDICE:** Barbara H. Billing and G. H. Lathe. *Am. J. Med.* **24**:111 (Jan.), 1958.

Recent progress made in bile pigment metabolism requires a change of nomenclature as well as classification of hepatic diseases. The old concepts of direct and indirect bilirubin has to be abandoned. The indirect bilirubin soluble in alcohol but insoluble in watery solution is true bilirubin. Solubility of this substance in water is obtained by ester linkage with glucuronic acid. Direct bilirubin, consists of two pigments, the monoglucuronide and the diglucuronide. Glucuronidation is the function of the liver cells and requires an enzyme, glucuronyl transferase. After experimental hepatectomy, however, there exists an extrahepatic mechanism for the conjugation of bilirubin glucuronide. Both bilirubin and conjugated bilirubin are normally transported in the blood attached to plasma albumin. Water soluble pigments

produce a greater degree of visible jaundice than equal amounts of nonwater soluble pigment. Chromatographic separation of mono- and diglucuronide may become useful in the differential diagnosis of jaundice. Neonatal jaundice, congenital hyperbilirubinemia and Gilbert's disease are caused by glucuronyl transferase deficiency. In the former condition the enzyme defect is only temporary while in the others it persists for a prolonged time, or is permanent. Kernicterus is caused by brain damage due to water insoluble bilirubin. Deficiency of glucuronidation is responsible for the accumulation of this pigment in the brain of children. Very jaundiced adults with well functioning enzyme mechanism do not get Kernicterus because the water soluble bilirubin is harmless.

H. B. EISENSTADT

**SCHULTZ-DALE TEST FOR DETECTION OF SPECIFIC ANTIGEN IN SERA OF PATIENTS WITH CARCINOMA:** D. Burrows. *Brit. M. J.* **5067**:368 (15 Feb.), 1958.

The search for a reliable and easily performed serological test for carcinoma is of

paramount importance. A test for carcinoma is described, which is based on two assump-

tions: 1. any carcinoma in the body will release into the circulation a substance specific to carcinoma tissue and not found in normal patients, and 2. it is possible to produce a reaction between this unknown substance and antibodies in a guinea-pig, which has been injected with carcinoma. The method used was a modification of Makari's method, which uses a very sensitive means of detecting antigen—the Schultz-Dale bath. The preparation of antibodies and all technical aspects of the test are described in detail.

Of 301 patients with carcinoma tested 291 or 96.7 per cent were positive. Of 207 patients without carcinoma tested, 200 or 96.7 per cent were negative. Ten patients, who had carcinoma surgically removed, were all negative two months postoperatively. If hemolysis is present, false positives are likely to be produced. The test was of no value with sarcoma, and it was impossible to produce antibodies in guinea-pigs for sarcoma.

**MULTIPLE ELECTROLYTE SOLUTIONS, THEIR USE IN PARENTERAL FLUID THERAPY: M. J. Sweeney. Illinois M. J. 113:4 (Jan.), 1958.**

The author gives a brief historical review of the development of multiple electrolyte solutions for use in parenteral fluid therapy.

A dosage of 1,500 ml. multiple electrolyte solution per square meter of body surface area per day will satisfy maintenance requirements. A dosage of 2,400 ml. will permit correction and electrolyte deficits secondary to past deficits, as well as furnish fluid requirements. A dosage of 3,000 ml. per square meter per day is

The test was not found to be a useful measurement of the amount of tumor present in the body, and was not found to be accurate in detecting tumors with a diameter of less than  $\frac{1}{2}$  inch (1.3 cm.) Some of the false negatives (tumor present, but not detected) were tumors, which had a strikingly large number of plasma cells around them. False positives were frequent in patients with nephrosis.

One cannot fail to be impressed by such a report, even after considering the limitations discussed by the author. This article brings to mind the recent hypothesis of Dr. Winston Price of Johns Hopkins, that all disease types may be detectable by serological methods. While we may be entering into a new phase of cancer-detection, these are early reports and therefore must be carefully evaluated and tested and retested, and hasty conclusions must be avoided. This is a promising, but very virgin field.

H. J. JOSEPH

needed for a severely dehydrated person, to correct past deficits and provide daily requirements. The amount can then be reduced according to the improvement.

Multiple electrolyte solution should not be used on patients with renal disease, adrenal insufficiency, patients with hypoparathyroidism, diabetes insipidus, heat exhaustion, or patients having suffered severe sodium chloride losses.

CARL J. DEPRIZIO

## BOOK REVIEWS FOR GASTROENTEROLOGISTS

**SYMPOSIUM ON GASTRODUODENAL ULCER AND CANCER INTERNATIONAL STUDY AMONG BLACK, BRONZE, WHITE, YELLOW, AZTEC, BANTU, BASA, BEDOUIN, ESKIMO, MAORI; RED-SKIN INDIAN, YAQUI, ZAPOTEAN PEOPLES:** Prof. Dr. William Nimeh, F.A.C.P. Volume I. 142 pages, illustrated. Catholic Press, Beirut, Lebanon, 1957.

This is an ambitious and extensive research of gastroduodenal ulcer in various races by a clinician, who deserves great credit for undertaking such a painstaking and complete exposé of a disease which is becoming more frequent year by year.

Opposite page 62, two illustrations, Figures 1 and 2, fail to explain what the author had in mind and opposite page 74, Figures 3 and 4 are upside down and also lack explanation.

A comprehensive discussion dealing with cancer is enlightening, as is a chapter on

"Diagnostic Significance of Radioactive Isotopes in Early Cancer of the Alimentary Tract" by Prof. Dr. Komei Nakaynia from the Chiba University School of Medicine, Japan.

Final chapters deal with the anatomy, physiology, and roentgenology of the stomach and duodenum.

Adequate references without a cross index complete the symposium. Despite the errors and omissions, it is a worthwhile edition to the library of the physician.

**ARTIOGRAPHY: ITS APPLICATION IN UROLOGICAL AND SOME OTHER CONDITIONS:** W. Barr Stirling, Ch.M., F.R.C.S. (Ed.), F.R.F.S.G., Senior Assistant Urologist, Urological Department, Glasgow Royal Infirmary, Consultant Urologist, Ministry of Pensions. 292 pages, illustrated. The Williams & Wilkins Company, Baltimore, Md., 1958. Price \$10.00.

Although the author states that this monograph is not intended as a book on urology or radiography, the reviewer finds it very interesting and suggests that clinicians as well as general surgeons will find a

great deal of useful suggestions in their daily practice.

The author and the publisher deserve credit for bringing out this authoritative and highly technical volume.

**ULCERATIVE COLITIS:** Harry E. Bacon, B.S., M.D., Sc.D., LL.D., F.A.C.S., F.A.P.S., Professor and Head of Department of Proctology, Temple University Hospital Medical Center, Philadelphia, Pa., President, American Board of Proctology; Diplomat American Board of Surgery and American Board of Proctology; Honorary Fellow, Royal Society of Medicine; Philippine College of Surgeons; International College of Surgeons; Brazilian College of Surgeons; Japanese College of Surgeons. Foreword by Alton Ochsner, B.A., M.D., Sc.D., F.A.C.S., F.A.P.S. (Hon.), Professor of Surgery, Tulane University School of Medicine; Director of Surgery, Ochsner Clinic and Ochsner Foundation Hospital, New Orleans, La.; Founder Member, American Board of Surgery; Past President, American College of Surgeons and American Cancer Society, with contributions by Paul T. Carroll, B.S., M.D. and chapter on Anesthesia by Leroy W. Krumperman, M.D., Professor and Head of Department of Anesthesiology, Temple University Medical Center, Philadelphia, Pa., American Board of Anesthesiology. 395 pages, 184 illustrated including color plate. J. B. Lippincott Company, Philadelphia, Pa., 1958. Price \$15.00.

With this array of talent, Bacon's "Ulcerative Colitis" must be good. In fact, the reviewer enjoyed reading the entire text and found it up to date and informative.

All practitioners of the healing art, plus laboratory workers will find valuable information between the covers, which will en-

hance their knowledge in dealing with various phases of colitis and its diagnosis.

A most interesting and instructive chapter, page 48, deals with ulcerative colitis, pseudopolyposis and carcinoma. One is struck with the positive assertion that polyposis or disseminated polyposis of heredo-

familial origin represents a distinct entity of adenomatous polyps and are precursors of carcinoma. According to Lockhart-Mummery, "all will eventually become cancerous if the patients live long enough".

Along with the above assertion, Bacon gathered statistics from various sources showing the tendency of ulcerative colitis to become associated with carcinoma and that the incidence of cancer of the large bowel has been shown to be considerably higher and develops at an earlier age in patients with ulcerative colitis than in the

general population. Another interesting statement is the frequent development of carcinoma following ileostomy. In summarizing, Bacon states that carcinoma of the rectum and the sigmoid in association with ulcerative colitis is more common than in other portions of the large bowel.

The reviewer can go on and on, however, he recommends that medical students, clinicians, surgeons and roentgenologists will well spend their leisure time in reading this informative volume and recommends it highly as a must.

**LES ASPECTS RECENTS DE L'ULCERE EXPERIMENTAL: From the Laboratory of Therapeutics of the Faculty of Medicine, Lyons, France (Prof. Levrat).** 480 pages, illustrated. Librairie Arnette, Paris, France, 1958.

As the title implies, this extensive volume deals with the recent aspects of experimental ulcer production. It should be of interest to laboratory researchers, biologists, biochemists and surgeons. The prescribing of hormones, antibiotics, cortisone and ACTH and their effect upon the gastric and duodenal mucosa, however, is of interest to the clinician.

Space does not permit me to go into de-

tail regarding the various experiments in animals and their relation to ulcer formation in man. It is, however, interesting to note the effect of aspirin and other salicylate-containing preparations as contributing factors in ulcer formation or aggravating previous dormant ulcers.

An extensive bibliography is appended. Translation into English is recommended.

**THE PSYCHOLOGY OF MEDICAL PRACTICE:** Mark H. Hollender, M.D., Professor and Chairman, Department of Psychiatry, State University of New York, Upstate Medical Center and Director, Syracuse Psychiatric Hospital with contributions by Leonard A. Stine, M.D., F.A.C.P., Assistant Professor, Clinical Medicine, Chicago Medical School; Attending Physician, Highland Park Hospital, Highland Park, Ill., Ernest M. Solomon, M.D., Instructor, Department of Obstetrics and Gynecology, Northwestern University Medical School, Chicago; Chairman, Department of Obstetrics and Gynecology, Highland Park Hospital, Highland Park, Ill. and Julius B. Richmond, M.S., M.D., Professor and Chairman, Department of Pediatrics, State University of New York, Upstate Medical Center, Syracuse, N. Y. 276 pages. W. B. Saunders Co., Philadelphia, Pa., 1958. Price \$6.50.

In the 10 chapters of this most instructive book, the author and his contributors have brought to the attention of the physician the doctor-patient relationship and what to tell the adult patient and the family. It is fascinating reading and is especially interesting to note on page 47, the conversation between the patient and the doctor and his spouse and on page 95, how should you tell a patient that he has cancer or when should you tell a patient that he has cancer, also is instructive.

Other chapters deal with surgical, obstet-

rical and pediatric patients as encountered in daily practice.

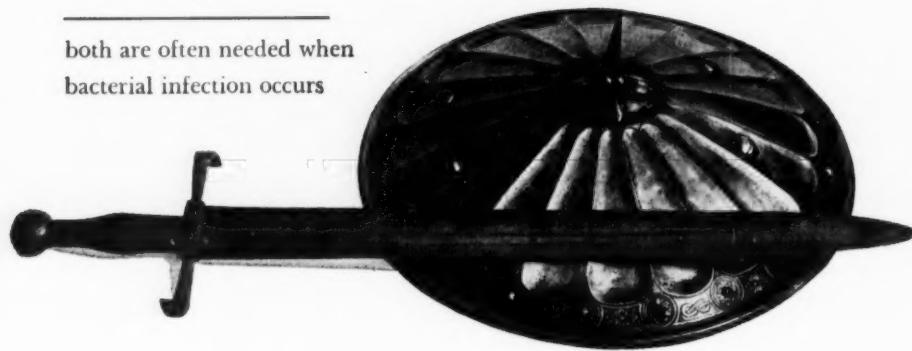
Very informative suggestions are found in chapter 19 dealing with the prescribing of medication, and in chapter 10, non-medical prescriptions conclude the text.

Ample references and cross index enhance the value of "Psychology of Medical Practice".

Every physician will probably want to own a copy and it is highly recommended by the reviewer.

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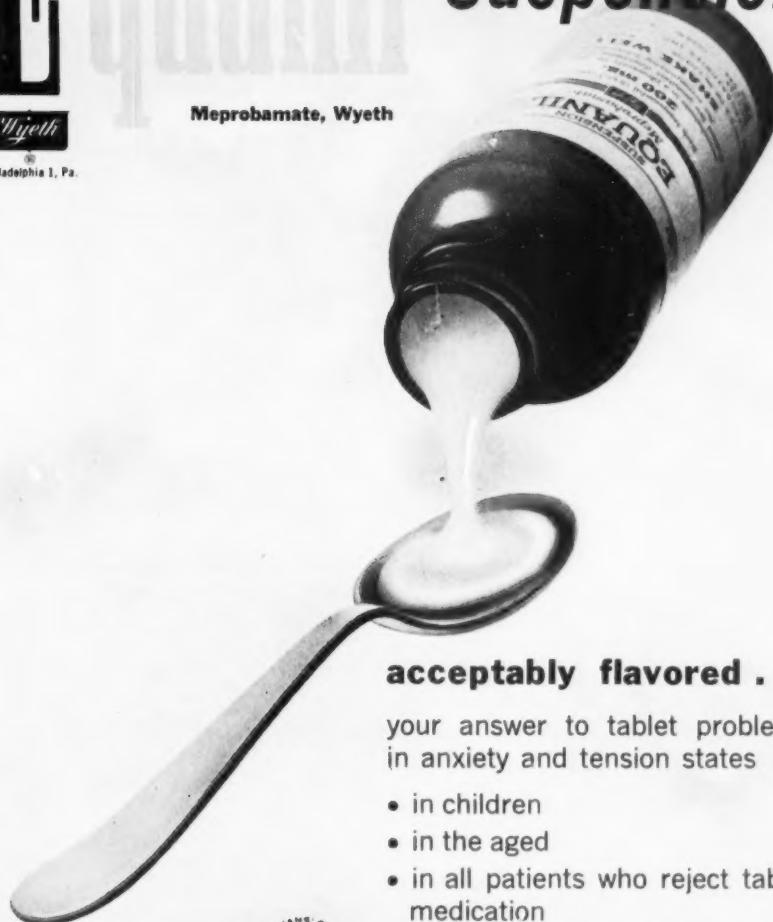
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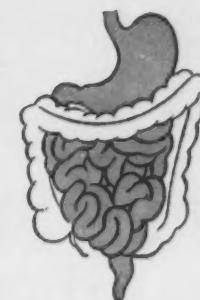
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See complete description in 1958 P.D.R.

(1) Kleckner, M. S., Jr.: J. Louisiana M. Soc. 108:359, 1956.  
(2) Riese, J. A.: Am. J. Gastroenterol. 28:541, 1957. (3) Settel, E.: J. Am. Geriatrics Soc., in press.

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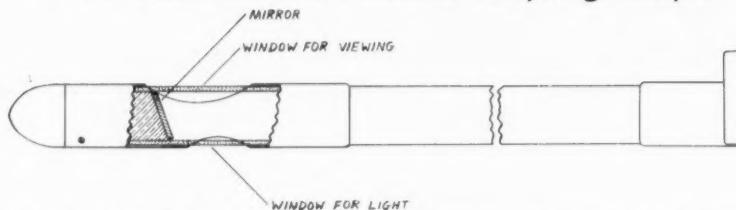
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<sup>1</sup>*American Journal of Gastroenterology*  
28:439, 1957.

<sup>2</sup>*British Medical Journal*  
2:827, 1955.

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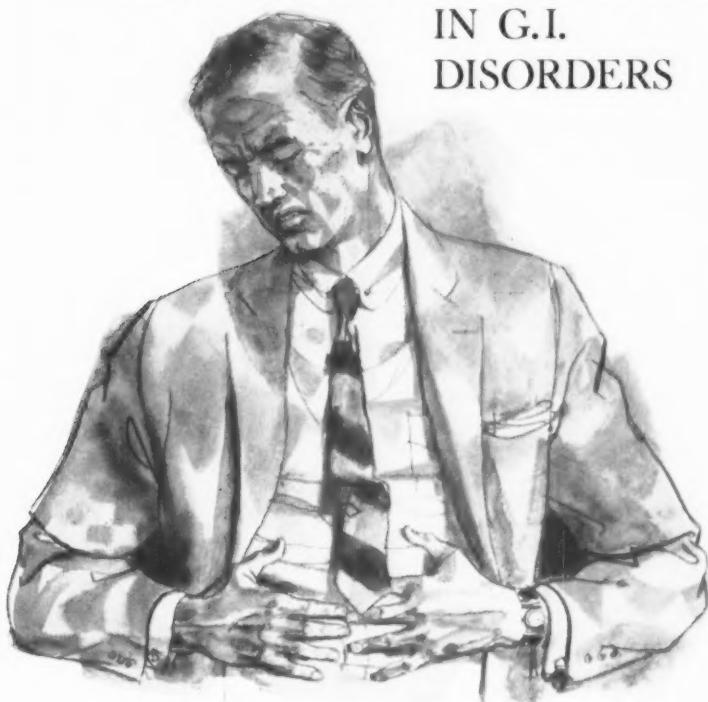
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1. Phillips, R. F.: *Am. Pract. & Digest Treat.* 7:1573, Oct. 1956. 2. Selling, L. S.: *J.A.M.A.* 157:1591, April 30, 1955. 3. Altshul, A. and Billow, B.: *New York J. Med.* 57:2361, July 15, 1957. 4. Ross, S. E.: *Postgrad. Med.* 27:24, Jan. 1958. 5. Tacket, H. S.: *Am. Pract. & Digest Treat.* 8:597, April 1957. 6. Bodl, T., Witts, C. W., Jr. and Menduke, H.: *Am. J. Gastroenterol.* 29:643, June 1958.

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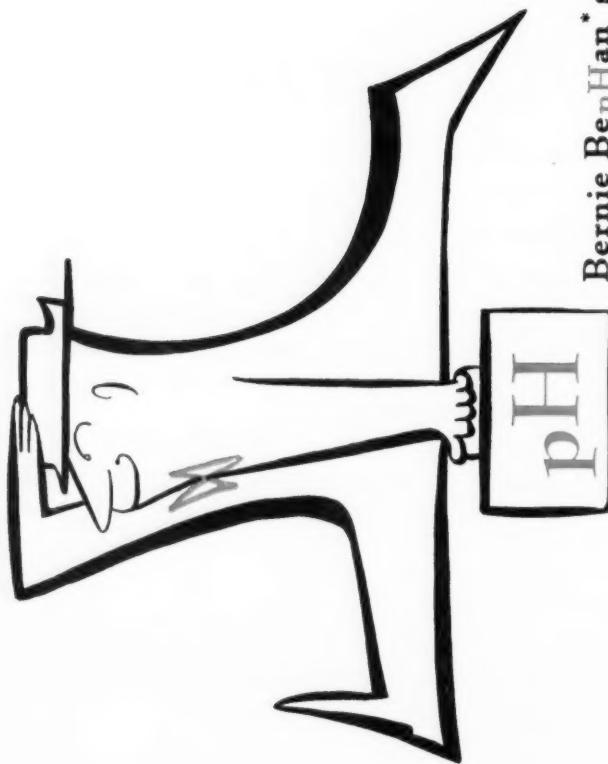
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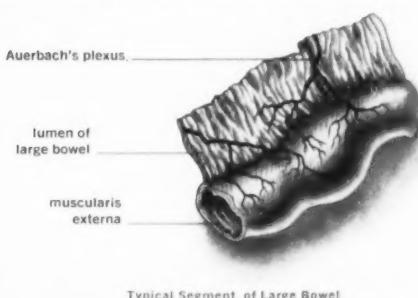
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**CITED REFERENCE:** 1. Herland, A.L., Lowenstein, A.: Quart. Rev. Surg. Obst. & Gynec. 14:196 (Dec.) 1957.

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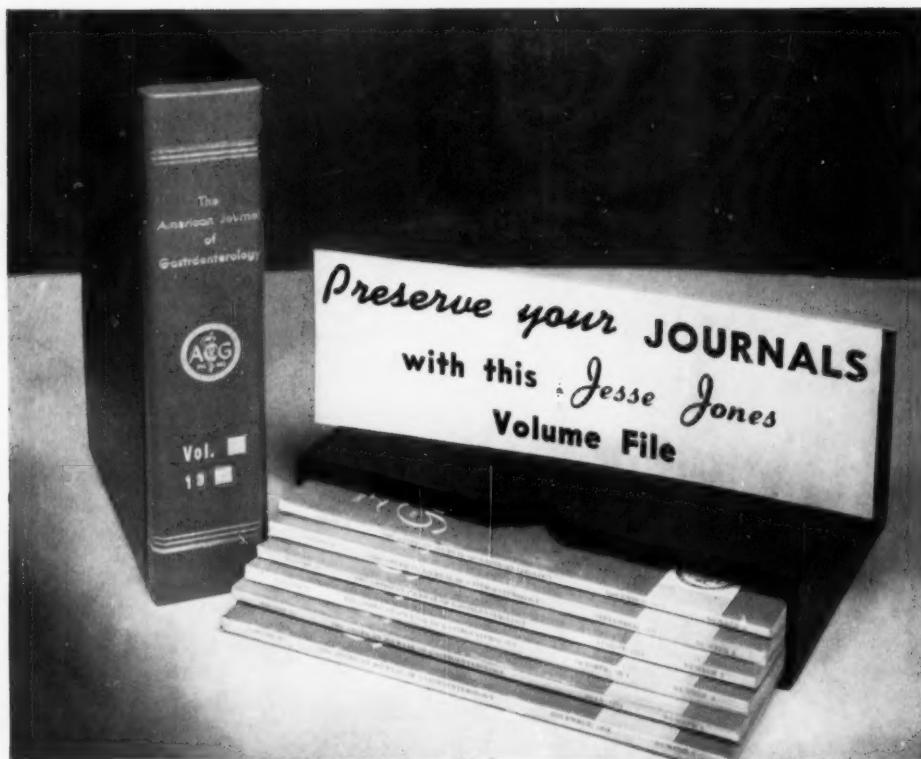


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Johnson, P. M. (Univ. North Carolina):  
Oral cholecystography,  
North Carolina M. J. 18:533, Dec., 1957.

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<sup>®</sup>Miltown + anticholinergic

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**G.I. dysfunction**

**INDICATIONS:** duodenal and gastric ulcer • colitis

• spastic and irritable colon • gastric hypermotility • gastritis • esophageal spasm

intestinal colic • functional diarrhea • G. I. symptoms of anxiety states.

**FORMULA:** each scored tablet contains: meprobamate 400 mg., tridihexethyl chloride 25 mg.  
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**DOSAGE:** 1 tablet t.i.d. with meals and 2 tablets at bedtime.

REPORTED FROM	NO. OF CASES	DIAGNOSES	RESULTS	SIDE EFFECTS	CONCLUSIONS
Texas	9	1 gastritis, 1 spastic enterocolitis, 2 spastic duodenitis, 1 duodenal ulcer, 1 G.I. symptoms of anxiety state, 1 gastric ulcer, 1 duodenal ulcer with pinpoint perforation-chronic, 1 cardiac neurosis with G.I. symptoms.	Marked improvement (9)	None (7) Drowsiness (1) Initial drowsiness (1)	4-excellent results, 1-good, 1-fine, 1-6 weeks' x-ray showed G.I. crater filled in and asymptomatic; tension disappeared, 1-symptoms completely ameliorated. 1-complete relief; on Milpath since the day it came out.
Ohio	15	7 G.I. symptoms of anxiety states, 4 duodenal ulcer, 2 spastic colon, 1 colitis-catarrhal, 1 diverticulosis.	Much improvement (1) Marked improvement (9) Slight improvement (4) Variable (1)	None (11) No answer (2) "Floating sensation" (1) Transient "lightheaded" feeling (1)	1-improvement over previous treatment, 2-well pleased, 1-was striking, 1-quite satisfied, 1-good, 1-was grateful, 1-better than any previous regimen, 1-indefinite, 2-very satisfactory, 1-undecided, 1-excellent, 1-"patient as well as myself was much impressed." 1—"Milpath therapy should be continued inasmuch as he has had ailment so long."
California	4	3 G.I. symptoms of anxiety states, 1 duodenal ulcer.	Marked improvement (3) Slight improvement (1)	None (4)	1-good, 3-satisfactory (1-continuing on decreasing dosage).
Idaho	5	1 gastro-enteritis of late pregnancy, 1 gastritis of late pregnancy, 1 chronic duodenal ulcer, 1 functional upper G.I. tract disease, 1 chronic gastro-duodenitis.	Marked improvement (5)	None (2) None of significance (2) Minimal drowsiness (1)	3-very effective, 1-believed to be of significant merit for upper G.I. distress of late pregnancy, 1-most effective medication used to date.
Illinois	5	2 hyperacidity, 3 peptic ulcer.	Marked improvement (5)	None (5)	2-excellent, 2-very good auxiliary treatment; 1—"of great importance in treatment of peptic ulcer."
Missouri	1	Pylorospasm.	Marked improvement	None	Effective G.I. antispasmodic.
North Carolina	15	10 pylorospasm, 2 duodenal ulcer, 1 possible Ca. of G.I. tract, 1 G.I. symptoms of anxiety, 1 gastritis-(alcoholic).	Marked improvement (11) Slight improvement (4)	None (14) Nausea (1)	12-very effective, 1-fairly good, 1-improved patient's condition, but did not solve the basic problem, 1-nausea (anomalous reaction).
Indiana	5	1 gastritis, 1 peptic ulcer (bleeding), 1 duodenal ulcer with gastritis, 1 duodenal ulcer, 1 psychoneurotic with gastric complications, insomnia.	Marked improvement (5)	None (3) Drowsiness (2)	1-excellent; patient has been feeling wonderful, 1-wonderful attitude on part of patient toward business life, 1-good, 2-excellent.
Oregon	10	3 gastritis, 2 spastic colitis, 3 G.I. symptoms of anxiety states, 1 healing duodenal ulcer, 1 herniation of pyloric mucosae.	Marked improvement (9) Slight improvement (1)	No side effects (6) Drowsiness (4)	9-very beneficial, 1-some improvement.
Florida	10	3 duodenal ulcer, 2 hypertrophic gastritis, 2 functional enterocolitis, 2 vomiting of pregnancy, 1 cardiospasm, meno-pausal syndrome.	Marked improvement (8) No improvement (2)	No side effects (9) Epigastric burning (1)	5-excellent, 1 no success, 3-very good, 1-inconclusive.
Michigan	10	1 spastic colitis, 2 gastrointestinal spasm, 1 colitis and diverticulitis, 1 duodenitis, 2 peptic ulcer, 2 duodenal ulcer, 1 gastric ulcer.	Marked improvement (8) Steady improvement (1) Slight improvement (1)	None (6) Some Dryness of Mouth (2) Drowsiness (2)	8-marked subjective and objective improvement, 1-encouraging improvement . . . patient has refused operation, so we are depending on this treatment, 1-steady improvement. Now on lower dosage and getting along well.

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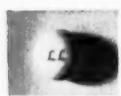


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